THESIS

FOR THE AWARD OF DEGREE OF

MASTER OF SURGERY (General Surgery)

SESSION 2020-2023

"CLINICO-PATHOLOGICAL FEATURES MANAGEMENT AND OUTCOME IN PATIENTS WITH CARCINOMA OF ORAL CAVITY – A CROSS SECTIONAL OBSERVATIONAL STUDY"

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"The roots of education are bitter, but the fruit is sweet"

- Aristotle

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Dr Nithin R. Pillai

Batch 2020-2021

ABBREVIATION

1. SCCOC	-	Squamous cell carcinoma of oral cavity
2. SCC	–	Squamous cell carcinoma
3. HSV	–	Herpes simplex virus
4. HPV	–	Human Pappiloma Virus
5. HIV	–	Human Immunodeficiency virus
6. AIDS	–	Acute Immune Deficiency Syndrome
7. OSMF	–	Oral Submucous fibrosis
8. IARC	–	International Agency for Research on Cancer
9. HIC	–	High income countries
10. LMIC	–	Low- middle income countries
11. WHO	–	World health organisation
12. OPD	–	Out patient department
13. TNM	–	Tumor Node metastasis
14. EUA	–	Examination under anesthesia
15. CT	–	Computed tomography
16. MRI	–	Magnetic Resonance imaging
17. PET	–	Positron emission tomography
18. OPMD	–	Oral potentially malignant disease
19. CI	–	Confidence interval
20. ADA	–	American dental association
21. END	–	Elective neck dissection
22. MRND	–	Modified radical neck dissection
23. SOHND	–	Supra omohyoid neck dissection
24. HNC	–	Head and neck carcinoma
25. OSCC	–	Oral squamous cell carcinoma
26. OVC	–	Oral verrucous carcinoma
27. TMA	–	Tissue microassay
28. HR	–	Hazard ratio
29. LNR	–	Lymph node ratio
30. DSS	-	Disease specific survival
31. CCRT	–	Concurrent chemotherapy
32. RT	–	Radiotherapy
33. OS	–	Overall survival
34. SES	–	Socio economic status
35. OTSCC	–	Oral tongue squamous cell carcinoma
36. AYA	–	Adolescent and young adult
37. DFS	–	Disease free survival
38. TND	–	Therapeutic neck dissection
39. RFS	–	Recurrence free survival
40. TT	–	Tumor thickness
41. TB	–	Tumor binding
42. DOI	-	Depth of invasion
43. PNI	–	Perineural invasion
44. OC	–	Oral cavity

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INTRODUCTION

INTRODUCTION

Head and Neck Cancers (HNC) are a major cause of morbidity and death in both the developed and developing countries. Every year, more than 500,000 people are diagnosed with HNC. HNC are categorised by both their anatomical location and their histopathology. Carcinoma of the oral cavity is one of the most common malignancies, especially in developing countries, but also in the developed world.

There are numerous risk factors that have been implicated in the oncogenesis of carcinoma of oral cavity, the most significant being tobacco and alcohol consumption. However, recently there has been an increasing number of Oral cavity carcinomas appearing in younger populations who have had less significant tobacco exposure. Several different explanations have been suggested for the cause of the cancers in these populations; however, there is yet to be conclusive evidence of the factors leading to carcinoma of oral cavity.

Oral cavity carcinoma is the 8th common carcinoma among men worldwide and ranks 14th among woman worldwide. Oral carcinoma is the common type of cancer in India in men and actually accounted for 40% of all forms of cancers. Squamous cell carcinoma (SCC) is the commonest histology and the frequant etiological factors are tobacco and alcohol consumption. Even when early diagnosis is relatively easy, presentation with advanced disease is not uncommon.

The basic modality of care is primary surgical resection of Tumor with or without postoperative adjuvant therapy. Advancements in surgical techniques combined with the routine use of postoperative radiation or chemoradiation therapy have resulted in improved survival statistics over the past few decades. Successful treatment of patients with oral cancer is predicated on multidisciplinary approach in treatment strategies to maximize oncologic control and minimize impact of therapy on aesthetic and function.

Cancer is by far the first and second commonest cause of mortality in developed and developing countries respectively [1]. The GLOBOCAN 2018 had given an estimation of 18.1 million fresh cases of cancer and 9.6 million deaths due to cancer in 2018, which was 14.1 and 8.2 million in 2012. Among all the cancers, Head and Neck Squamous cell carcinoma (HNSCC) presents with 600,000 cases worldwide, with 40–50% mortality annually and the burden is estimated to near double in developing countries by 2030. A majority these Tumors arise from the epithelial cells of oral cavity (OC), oropharynx, larynx or hypopharynx. Oral squamous cell carcinoma

(OSCC) has the highest prevalence in the HNSCC group accounting to be 11th and 18th commonest cancer worldwide as per 2012 and 2018 data respectively. The overall global decrease in the prevalence of OSCC is associated with the lesser tobacco chewing habits and geographic heterogeneity, however, it is still the commonest cancer in South Asia, South Central Asia as well as the Pacific Islands (Papua New Guinea, with the highest incidence worldwide in both sexes]. In 2018, India alone had estimated 120,000 new patients diagnosed out of which approximately 72,000 patients died. Taiwanese region had also presented with the world's highest incidence of OC carcinoma which were accounted for 8% of all new cancers diagnosed and 6.3% of all carcinoma deaths in 2014. In the south Asian subcontinent, this cancer ranks first in Bangladeshi and Pakistani males.[2]

The anatomy of OC is vital because of proximity of structures and for long time carcinomas of oral cavity and oropharynx were clubbed as OSCCs which also varied the epidemiological data. Advanced translational and clinical researches have been able to differentiate both in many aspects recently. Tumors of oropharynx constitutes the base of tongue, palantine tonsils, soft palate and adenoids but OC starts anteriorly from the vermillion of the lips and extends posteriorly to circumvallate papillae of the tongue consisting of the alveolar ridge and gums, alongwith the anterior two-thirds of the tongue, floor of the mouth, buccal mucosa, retromolar trigone, and hard palate.[3] Amongst OSCC subsites, tongue and buccal cavity cancers are more common followed by lip and palate. The risk factors of OSCC vary with geographic location including which include smoking, alcohol, chewing tobacco, and infection with human papillomaviruses (HPVs) among others.

Lip and OC cancer were the 2nd commonest cancer in Pakistan if both genders are combined [10.9%] and first in males with 15.9% fresh cases. This rise in the burden is associated with the augmented use of areca nut or any type of smokeless tobacco (SLT). SLT is a group of more than 30 products that differs in their toxicity and addictiveness depending upon the composition. The classic chewing substances are betel quid (commonly known as paan contains betel leaf, slaked lime, areca nut, and tobacco), gutka (consists of areca nut, tobacco, paraffin wax, slaked lime, and any flavoring) pan masala (slaked lime, areca nut, tobacco, musk ketones), naswar (containing tobacco, ash, lime], tobacco, mainpuri, and mawa [made of tobacco, lime, and areca nut). These substances contain nearly 28 known carcinogens amongst which arecoline, nonvolatile alkaloid-derived, nitrosamines, volatile aldehydes, flavonoids and tannins are of prime importance [4]. All these carcinogenic compounds change the normal morphology of the cells thus inducing cytogenetic or genetic alternations. Low socioeconomic

status (SES) has predictive significance specifically for HNSCC and an increased incidence has been reported in low-income countries. In the local context, the frequency of chewing habits has also been shown in association with low socioeconomic backgrounds, education, and is more prevalent in males. Challenged with such a high burden of OSCC in our population, there is a relative deficiency of information regarding the prevalence and association of these habits with OSCC and low SES in recent period.

REVIEW

OF

LITERATURE

REVIEW OF LITERATURE

ANATOMY OF THE ORAL CAVITY

The oral cavity starts from the vermilion border of the lips to the circumvallate papillae of the tongue inferiorly and the junction of the hard and soft palate superiorly. The oral cavity is further divided into several anatomical subsites: lip, oral tongue, floor of mouth, buccal mucosa, upper and lower gum, retromolar trigone and hard palate. Even when their proximity, these subsites have distinct anatomical characteristics that need to be taken into consideration in planning oncologic therapy.

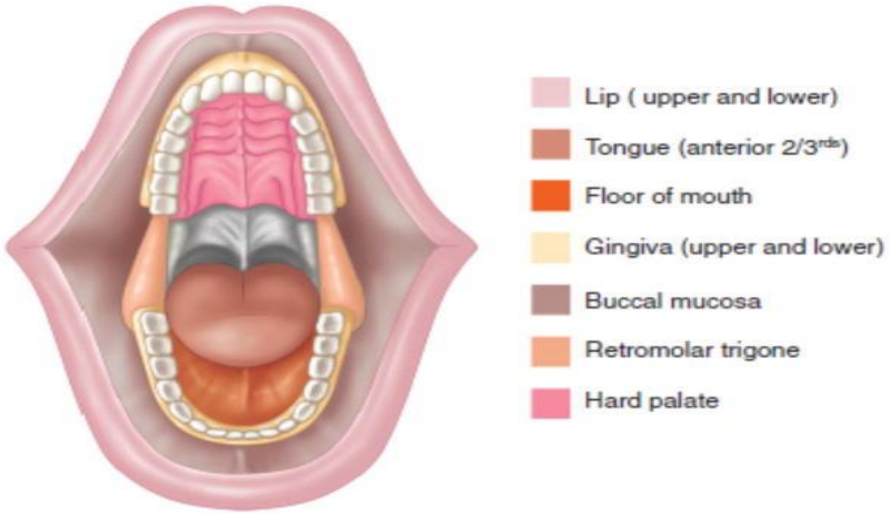

Figure 1 Anatomic sites of the oral cavity

Oral Vestibule

The oral vestibule is boundaried outside by the lips and the cheek mucosa and internally by the alveolar processes and the teeth. While the teeth are in occlusion, the vestibule communicates with the oral cavity proper through the intermaxillary commissure posterior to last molar teeth.

Lips

The longer upper lip and shorter lower lip are connected one another by the labial commissures at the corners of the mouth. The lips are parted from cheeks by the nasolabial fold. The lip constitutes a pale wet vermilion inside and an outer darker dry vermilion, separated from each other by the red line; there is another white line externally that is the purely cutaneous part of the lip.[5]

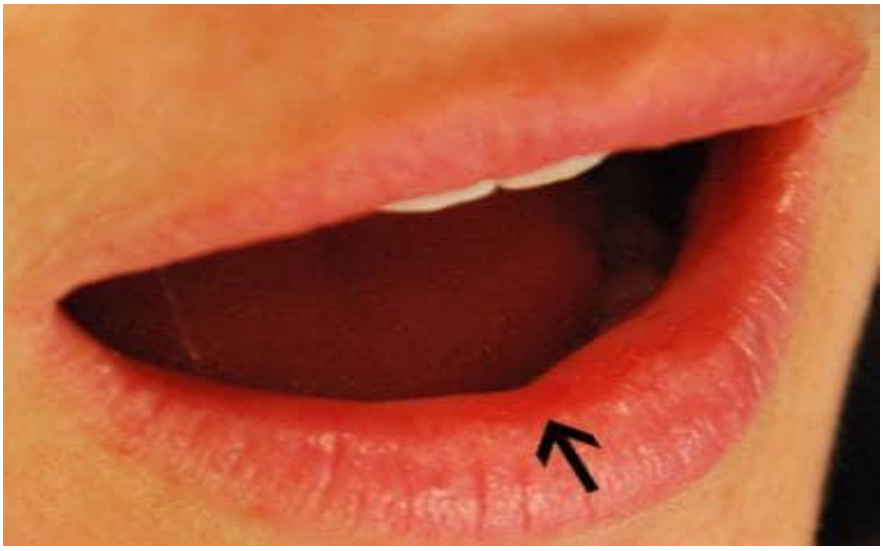

Figure 2 Vermilion of lip

Cheek

The cheek is a musculomembranous structure, limiting superiorly and inferiorly by superior and inferior vestibules, anteriorly by labial commissure, and posteriorly by retromolar trigone and the inter-maxillary commissure. The inner surface of both lip is connected in the middle line to the corresponding gum by a fold of mucous membrane known as the labial frenulum. The upper labial frenulum is larger than the lower labial frenulum.[6]

Figure 3 Upper vestibule (upper lip everted). Arrow indicates upper labial frenulum.

Figure 4 Lower vestibule (lower lip everted). Arrow indicates lower labial frenulum

The retrocommissural region is sited in between the labial commissure and the orifice of Stensen’s duct, situated opposite the second upper molar. Stensen's duct runs via the buccinator muscle. A horizontal mildly elevated streak known as the linea alba traverses this region. It level with the biting plane.

Figure 5 Opening of Stensen's duct opposite second upper molar (arrow). Asterisk indicates retromolar trigone.

Figure 6 Linea alba (arrow).

The buccinator muscle forms the muscular framework of the cheek which functions for facial expression also which is covered by the buccal fat pad, that smoothes the contour of cheek by compensating the depression and the anterior border of the masseter. The masseter muscle lays over the buccinator. Other muscles contribute to the development of the cheek, such as the zygomaticus, risorius, and platysma.

Gums and alveolar process

The gingiva is a fibroepithelial mucosal tissue that lays around the teeth and bounds the alveolar jawbone.The alveolar process is the tooth-bearing site of the jaws. It is made of a dense outer cortex which is known as the cortical plate and looser inner medullary bone. The area of cortical bone that lines the alveolus is called the lamina dura.

Retromolar trigone

The retromolar trigone is a small triangular formed subsite of the oral cavity. It is the portion of mucosa that lies posterior to the third molar tooth, covering the anterior rami of the mandible. The base of the triangle lies posterior to the last lower molar tooth. The apex is in line with the tuberosity of the maxilla posterior the last upper molar tooth. The retromolar trigone is boundaried laterally by the gingival buccal sulcus and medially by the anterior tonsillar pillar.

Teeth

The teeth are calcified structures functions in mastication. Each tooth is framed of a crown, which is the outward portion above the gumline, and a root, which is buried in the jawbone.

Deciduous teeth are the initial ones to emerge in the oral cavity and are progressively replaced by the adult dentition. There are nearly 20 deciduous teeth, comprising of 8 molars, 4 canines and 8 incisors. The permanent dentition consists of 32 teeth: 12 molars, 8 premolars, 4 canines, and 8 incisors.

Incisors have thin occlusal edges, a sort of flat crown, and a single root. Their main purpose is to fragment food. Canines have a pointed shape and single long roots functions is to pierce and tear food.

The masticatory surface of molars and premolars is characterized by sharp structures named cusps. Premolars basically consists of 1 or 2 cusps and 1 or 2 roots. Molars on the other hand consists of 4-5 cusps and 2-3 roots, the shape of which is highly variable. The function of molars and premolars is to grind and crush food for easy deglutition.

Gross Anatomy: Oral Cavity Proper

Hard palate

The palate is a horseshoe-shaped, domed roof of the oral cavity. It is divided into a hard part and a soft part. The hard palate belongs to the oral cavity that separates it from the nasal cavities. The soft palate belongs to the oropharynx and divides it from the nasopharynx.

The hard palate is concave, which concavity is occupied mostly by the tongue when it is at rest. The hard palate is further divided into primary and secondary palates. The primary palate is separated from the secondary palate through a small depression posterior to the central incisors termed the incisive fossa, where the incisive foramen emerges.

The anterior two thirds of the hard palate is formed by the incisive bone premaxilla, and the palatine processes of the maxilla. The horizontal plate of the palatine bone form the posterior third of the hard palate. The secondary palate presents a midline raised suture line known as palatine raphe. Also the hard palate also has transverse ridges on the anterior third that serve to retain the food bolus.

Soft palate

The soft palate marks the beginning of the oropharynx and is the mobile posterior one third of the palate. It forms an incomplete septum between the oral cavity and the oropharynx. It is demarcated by a median raphe and is in continuity with the roof of the mouth and the mucous membrane of the nasal floor.

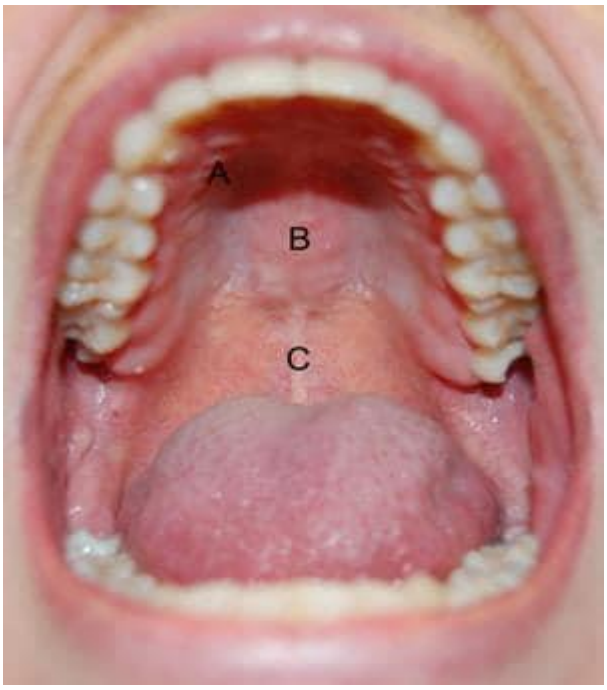

Figure 7 Soft and hard palate

When the soft palate is in a relaxed state, its anterior surface is concave and its posterior surface is found convex. The anterior aponeurotic portion is adhered to the posterior border of the hard palate, and the posterior muscular portion that hangs between the oral cavity and the oropharynx which is termed the palatine velum.[7]

The velum is elongated by a median free process known as the uvula and 2 bilateral processes known as the palatoglossal and palatopharyngeal arches or pillars, which connects the soft palate to the tongue and pharynx.[7] The fauces denotes the area between the cavity of the mouth and the oropharynx. They are boundaried superiorly by the soft palate, inferiorly by the root of the tongue, and laterally by the faucial pillars.

The palatine tonsils are situated in the tonsillar fossae of the oropharynx, which is bordered by the palatoglossal and palatopharyngeal arches and the tongue.[7]

During deglutition, the soft palate is primarly tensed to churn the bolus of food between the tongue and pharynx before raising of the soft palate to obstruct the nasal passages while the bolus is pushed into the pharynx.

Floor of mouth

The floor of mouth forms the inferior boundary of the oral cavity. It is usually compared to a quadrangular pyramid with a posterior base. Generally, it is divided into 3 zones: the anterior floor of the mouth located anterior to the lingual frenulum and the 2 sublingual folds situated among the lateral tongue and the mandibular gingiva.

The sublingual papillae which is referred to as caruncles or folds can be identified on either side of the frenulum in the anterior part of the floor of mouth when the tip of the tongue is raised. The Wharton's duct runs in the floor of the mouth along the medial border of the sublingual gland to open into the surface of the mouth at the paramedian sublingual caruncle. The sublingual glands have numerous small ducts that drain straight into the floor of the mouth.

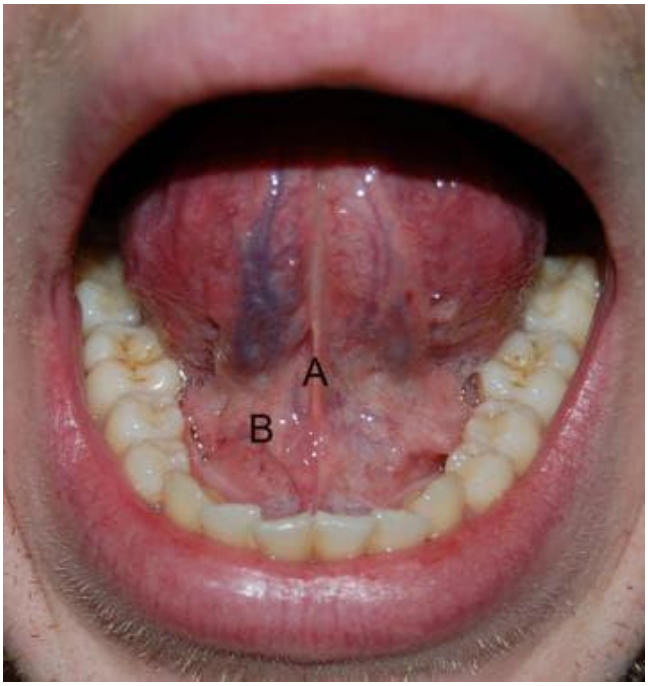

Figure 8 Tongue and major salivary glands

Tongue

The tongue is a mobile muscular organ that beholds the major part of the oral cavity and part of the oropharynx. Its main functions are propelling food into the oropharynx during

swallowing and articulation of words during speaking, although it is also implicated in mastication, taste, and oral cleansing.

The major salivary glands are large paired exocrine glands that communicate with the mouth and directs their secretions into its cavity. They namely the parotid, submandibular and sublingual glands.

Microscopic Anatomy

As food is physically fragmented in the oral cavity, this region is lined by a protective, nonkeratinized, stratified squamous epithelium, which also lines the mucosal aspect of the lips. The oral cavity proper is layered by a masticatory mucosa which is gingiva and hard palate, a lining mucosa in the lips, cheeks, alveolar mucosal surface, floor of the mouth, inferior surface of the tongue, and a specialized mucosa on the dorsal surface of the tongue. [8]

Lips

The outer lip (outer vermilion) is lined by skin. The epidermis is composed of stratified squamous, keratinized epithelium. Under the epidermis, the dermis is consists of sebaceous glands, hair follicles, sweat glands, arrector pili muscles, and the neurovascular bundle on the lip periphery.

The mucosal lip (interior vermilion) is lined with a stratified squamous, nonkeratinized epithelium. Beneath the epithelium is a lamina propria, the counterpart of the dermis. Tubuloacinar labial glands are present in the submucosa. These are mostly mucous; their secretion moistens the oral mucosa, and their finer ducts open into the oral cavity. The core of the lip contains fibers of striated orbicularis oris muscle.

Cheeks

Lining mucosa is seen on the cheeks. It is covered by striated muscle and major salivary glands. The epithelium of the lining mucosa is nonkeratinized, but at times in some places it can be parakeratinized. Parakeratinized epithelium is like keratinized epithelium, except that the superficial cells are not devoid of their nuclei.

The nonkeratinized epithelium is thicker than keratinized epithelium. It consists of a stratum basale, a stratum spinosum, and a stratum superficiale. The cells of the mucosal epithelium consists of keratinocytes, Langerhans cells, melanocytes, and Merkel cells.

The underlying lamina propria is a thick papillary layer of loose connective tissue that is composed of blood vessels, nerves that send axon endings to the epithelium, and encapsulated sensory endings in few papillae. The lining mucosa has scarce and shorter papillae so that it can adjust to the movement of its underlying muscles.

The distinct submucosa of the lining mucosa consists of large bands of collagen and elastic fibers that bind the mucosa to the underlying muscles. It also consists of many minor salivary glands of the lips, tongue, and cheeks, which are mostly mucous. The submucosa is composed of larger blood vessels, nerves, and lymphatics that supply the lamina propria.

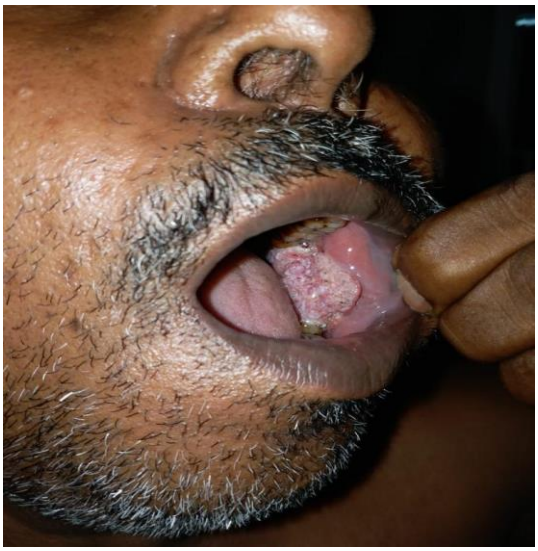

Figure 9 Carcinoma of Buccal Mucosa

Teeth

The teeth are composed of 4 unique tissues. The crown is covered with a layer of enamel, a highly calcified and acellular tissue. The enamel is the considered hardest tissue of the body.

The central portion of each tooth is made of the second tissue, the pulp. The pulp is a fibrovascular tissue consisting of odontoblasts whose function is innervation, vascularization, and repair.

Under the enamel and around the pulp lies the dentin, which adds to the bulk of each tooth. The dentin contains calcified tissue consisting of numerous microscopic channels known as dentinal tubules, which harbor odontoblastic processes.

The fourth dental tissue, cementum consists of a very thin layer of calcified tissue covering the dental root. The apical portion of the tooth is covered by cellular cementum, where the rest is

coated by acellular cementum. The cementum is adhered to the alveolar bone via specialized connective tissue fibers, which form the periodontal ligament.

Gums and alveolar process

The gums are layered with masticatory mucosa. This mucosa has a keratinized and parakeratinized stratified squamous epithelium. The underlying lamina propria harbours blood vessels, sensory receptors and Meissner's corpuscles. Beneath the lamina propria is a reticular layer of dense connective tissue. The reticular layer blends with the periosteum; thus, no submucosa is in existance.

Hard and soft palate

The hard palate is also layered with masticatory mucosa. In the palatine raphe, the mucosa also bind firmly to the periosteum, and no submucosa exists. In the other areas of the hard palate, a submucosa that consists of thick collagenous bands extending from the mucosa to the bone underlies the lamina propria. The submucosa consists of adipose tissue anteriorly and mucous glands posteriorly.

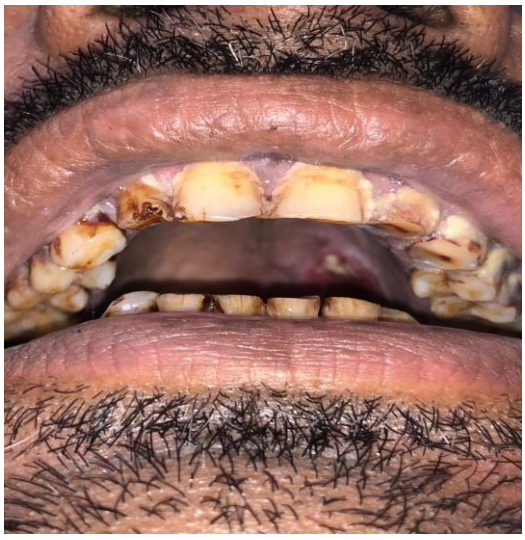

Figure 10 Carcinoma of Hard palate with trismus

Minor salivary glands

The basic architecture of a salivary gland is that of a branching duct that has the principal secretory cells called the acinar cells at the proximal ends of the branches and an opening onto the oral cavity on the other end of a single collecting duct. Four morphologically and functionally different segments exist in each basic salivary gland unit known as acinus,

intercalated duct, striated duct, and excretory duct. Two types of cells exist in each segment namely abluminal cells and luminal cells.

The abluminal cells are basically myoepithelial cells in the acinus and intercalated duct and basal cells in the striated and excretory ducts. Acinar cells can be serous or mucous, based on the chemical composition of the saliva produced by a specific gland. Parotid glands are mostly serous, submandibular glands are mixed but predominantly serous, sublingual glands are mixed but predominantly mucous, and minor salivary glands are mixed which are predominantly mucous, except in when in the palate, where the glands are mostly mucous, and in the tongue.[9]The oral cavity is distributed with 500-1000 minor salivary glands with in the mucosa and submucosa of the cheeks, lips, floor of the mouth, hard and soft palates, retromolar trigone, and tongue whereas they are absent in the anterior hard palate and gingivae.

The lobules of the minor salivary glands are of 1-5 mm in size and are parted from one another by connective tissue. Glands in the posterior hard palate are more plenty and more confluent. Most lobules have individual excretory ducts that directs and emerges into the oral cavity, but they are not usually perceivable.[9] In the tongue, lips, and buccal mucosa, lobules of salivary gland tissue are situated under the mucosal epithelium and with in the deeper skeletal muscles. These glands are basically unencapsulated. [9]The posterior hard palate contains pure mucous type acini without serous cells. In the tongue, Blandin and Nunn glands are situated on the anterior ventral part and are of mucous type. The posterior dorsal and lateral portions contain serous glands known as von Ebner glands. [9]

Musculature of Mastication

The movements of the mandible are mainly aided by the 4 muscles of mastication: the masseter, temporalis, lateral pterygoid, and medial pterygoid muscles. All of these muscles comes from the mesoderm of the first pharyngeal arch, and their innervation is by the anterior trunk of the mandibular nerve (cranial nerve V3).

The masseter is a quadrangular muscle that has two parts; deep part and a superficial part. The deep portion arises from the inferior surface of the zygomatic arch and descends almost vertically to insert onto the lateral surface of the ramus. The superficial portion arouses from the zygomatic bone anterior to the temporozygomatic suture and descends down and back to get insert onto the angle of the mandible. The action of the masseter is mandibular elevation. Some superficial fibers have a limited role in mandibular protrusion.

The temporalis is a broad triangular muscle that origins from the floor of the temporal fossa and from the deeper plane of the temporal fascia. It inserts on the tip and medial aspect of the coronoid process and on the anterior border of the ramus of the mandible. Its main action is to raise the mandible. Some horizontal fibers are involved in mandibular retraction.

The lateral pterygoid muscle is a 2-headed triangular muscle that has 2 seperate origins: the infratemporal surface and crest of the greater wing of the sphenoid and the lateral surface of the lateral pterygoid plate. The upper head gets inserted onto the joint capsule and articular disc of the temporomandibular joint. The inferior head gets inseted to the anteromedial aspect of the neck of the condyle. Bilateral contraction of this muscle functions in protraction of the mandible and depression of the chin. Unilateral contraction makes the jaw move contralaterally.

The medial pterygoid muscle is also a 2-headed muscle; it arises from the medial aspect of the lateral pterygoid plate and the pyramidal process of the palatine bone and from the maxillary tuberosity. It gets inserted onto the medial surface of the ramus of the mandible. Its main function is mandibular elevation, in synergy with the masseter muscle. It also facilitates mandibular protrusion.

Mandibular depression is mainly facilitated by gravity. The suprahyoid and infrahyoid muscles, whose chief roles are to elevate and depress the hyoid bone and the larynx, respectively, may also facilitate mandibular depression.

Blood Supply and Lymphatic Drainage

Blood is supplied to the oral vestibule and oral cavity through branches of the external carotid artery such as facial, maxillary, and lingual. The terminal branches of the arteries often anastomose freely, along with anastomoses across the midline to their contralateral partners.

The facial artery supplies the major arterial supply to the lips. It branches out as superior and inferior labial arteries 1 cm lateral to the corner of the mouth. The superior labial artery supply the upper lip. The inferior nasal artery provide supply to the lower lip. These arteries anastomose among themselves to form an arterial ring.

The angular artery which is a terminal branch of the facial artery, supplies the superior part of the cheek. The facial vein provides drainage to the lips. It conjoins with a communication of

the retromandibular vein to form the common facial vein and drains into the internal jugular vein at the level of the hyoid bone.

The maxillary artery is the largest of the 2 terminal division of the external carotid supplying the cheek mucosa, teeth, gingivae, and palate. It originates posterior to the mandibular neck and is at first embedded in the substance of the parotid gland. As it emerges, it is sub divided into 3 parts: mandibular, pterygoid, and pterygopalatine.

The mandibular portion of the maxillary artery gives off the inferior alveolar artery, which penetrates the mandible and supplies the mandibular teeth, chin, and mylohyoid muscle. The pterygoid portion divides out into the masseteric artery, which supply the masseter. The deep temporal arteries, supplies the temporalis muscle. The pterygoid branches supplies the pterygoid muscles and the buccal artery, supplies the buccal fat pad, buccinator, and buccal oral mucosa.

The pterygopalatine portion of the maxillary artery divides into posterior superior alveolar artery, infraorbital artery, artery of the pterygoid canal, pharyngeal branch, descending palatine artery, and sphenopalatine artery.

The maxillary molar and premolars and the adjacent gingiva is supplied by the posterior superior alveolar artery. The infraorbital artery perfuses the maxillary canines and incisors and the skin of the infraorbital area of the face. The descending palatine artery descends down the palatine canal and branches out as the greater and lesser palatine arteries to supply the mucosa and glands of the hard and soft palate. The sphenopalatine artery travels through the sphenopalatine foramen to supply the anteriormost palate. [7]

Innervation

Sensory innervation to the lips, cheeks, gingivae, teeth, hard palate, and floor of the mouth is facilitated by the trigeminal nerve, more precisely the maxillary [V2] and mandibular [V3] divisions of this nerve. Branches of V3 also innervates the 4 muscles of mastication, but the motor supply of the buccinator and orbicularis oris muscles is by the buccal branch of the facial nerve.[7]

In the upper jaw, the buccal and gingival mucosa are innervated by the maxillary and mandibular divisions. In the lower jaw, they receive supply from the mandibular division.

The maxillary nerve [V2] exits the cranium through the foramen rotundum in the sphenoid and emerges into the pterygopalatine fossa, where it gives off branches to the pterygopalatine ganglion and proceeds to the inferior orbital fissure. It gives off the zygomatic nerve and rides through the infraorbital groove as the infraorbital nerve.[7]

The posterior and middle superior alveolar nerves originates from the maxillary nerve, and the anterior superior alveolar nerve originate from the infraorbital nerve. These nerves supplies the maxillary molars. The gingival branch originates from the posterior superior alveolar nerve and innervates the mucosa of the gingiva and of the cheek near the upper molars.

The infraorbital branch of the maxillary nerve divides as palatine branches. This nerve also innervates the mucosa of the upper lip and labial vestibule. The mandibular nerve [V3] descends down the foramen ovale into the infratemporal fossa and branches as the auriculotemporal, inferior alveolar, lingual, and buccal nerves.

The inferior alveolar nerve emerges into the mandibular foramen, rides through the mandibular canal, and generates the inferior dental plexus. The inferior dental plexus guides branches to all mandibular teeth on its side. The mental nerve is another division of the plexus that innervates the skin and mucous membrane of the lower lip and the vestibular gingiva of the mandibular incisors. The lingual nerve locates anterior to the inferior alveolar nerve and gives sensory supply to the floor of the mouth and the lingual gingiva. [7]

EPIDEMIOLOGY AND ETIOLOGY

Worldwide, 405,000 new cases of oral carcinoma are predicted each year, and the countries with the highest incidence are Sri Lanka, India, Pakistan, Bangladesh, Hungary and France. In the European Union there are an estimated 66,650 fresh cases each year. The American Carcinoma Society estimates that there will be approximately 42,440 new carcinomas of the oral cavity and oropharynx in the U.S. leading to 8,390 deaths in 2014. Tobacco smoking and alcohol are the commonest etiological factors in SCC of the oral cavity (SCCOC). Other habits such as betel nut and tobacco chewing have been seen in the Asian population.

Tobacco contains numerous carcinogenic molecules like polycyclic hydrocarbons and nitrosamines. A directly constitutional impact exists between the pack years of tobacco used and the risk of SCCOC. This risk declines after tobacco cessation, but it does not fully abate (30% in the first 9 years and 50% for those over 9 years). A decreased incidence of oral cavity

carcinoma has been reported in the last 15 years, widely attributed to a decline in tobacco consumption.

Alcohol and tobacco have a synergistic effect on the etiology of oral and oropharyngeal SCC. However, alcohol is associated to an increased risk of carcinoma on its own even in non-smokers. Other factors such as inadequate oral hygiene, wood dust exposure, dietary deficiencies, red meat and salted meat consumption had been reported as etiologic factors. The herpes simplex virus (HSV has been suspected but have not been recently implicated in the etiology of SCCOC. Upon the emerging evidence supporting the role of the human papilloma virus (HPV) in the etiology of oropharyngeal carcinoma, it has been conclusively associated with SCCOC. Host factors such as immune system alterations in transplant patients and HIV-infected patients with AIDS and genetic conditions such as xeroderma pigmentosum, fanconis anemia and ataxia telangiectasia are associated with an increased occurence of head and neck carcinoma.[11]

Oral carcinoma is more common in men and occurs after the 5th decade of life. About 1.5% will have another synchronous primary in the oral cavity or in the adjacent aero-digestive tract (larynx, esophagus or lung). Metachronous Tumors develop in 10% to 40% in the first decade after treatment of the index primary [12] and therefore timely post-therapy surveillance and lifestyle alteration are utmost important strategies for secondary prevention.

Smokeless and Smoking Tobacco Use

Smokeless tobacco in the form of betel quid, oral snuff, and betel quid substitutes heightens the risk of oral precancerous lesions and oral carcinoma between 2-15fold.[15] In most areas, betel quid composed of tobacco, areca nut, slaked lime, catechu, and several condiments, wrapped in a betel leaf. In recent times, small, fancy and inexpensive sachets of betel quid substitutes consisting of a flavored and sweetened dry mixture of areca nut, catechu, and slaked lime with tobacco [gutkha] or without tobacco [pan masala], often claiming to be safer products to consume, have become widely available and are seen increasingly consumed by young population, especially in India. These products have been strongly associated with oral submucous fibrosis (OSMF), which places individuals at higher risk for malignancy.

More than 50 % of oral carcinomas in India, Sudan, and the Republic of South Sudan, and about 4 % of oral carcinomas in the United States, are associated with smokeless tobacco products. Smokeless tobacco use among young population is increasing in South Asia, with

the marketing of conveniently packaged products made from areca nut and tobacco; as a result, oral precancerous conditions in young adults have increased drastically.[15]

Consistent evidence from multiple studies suugests that tobacco consumption in any form increases the risk of oral carcinoma by 2-10 fold in men and women (IARC 2004a). Risk increases significantly with time and frequency of tobacco consumption. Risk among reformed smokers is consistently lower than among active smokers, and there is a trend of decline in risk with more number of years since quitting. Use of smokeless tobacco and alcohol in combination with tobacco smoking syergestically increases the risk of oral carcinoma. The biological plausibility is provided by finding out several carcinogens in tobacco, the most abundant and strongest being tobacco-specific N-nitrosamines, such as N-nitrosonornicotine and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone. These are formed by N-nitrosation of nicotine, the major alkaloid leading to addiction for tobacco.

The fact that not less than 80 % of oral carcinomas are associated with tobacco and/or alcohol consumption justifying regular oral examinations targeting tobacco and alcohol users, as well as prevention efforts aiming on tobacco and alcohol control. The World Health Organization Framework Convention on Tobacco Control, an evidence-based international treaty, focusing on reducing the demand for tobacco globally by price, tax, and non-price measures.

Areca Nut Chewing

Areca nut also known as betel nut because it is often wrapped in betel leaf, is now considered as a type 1 carcinogen (IARC 2004b, 2007). It is consumed and chewed raw, dried, or roasted, or as part of betel quid, by lakhs of people in Asia. Its consumption is spreading across the Pacific and also among emigrant Asian communities worldwide. Cheap and easy to access, prepackaged areca nut products, such as pan masala, are of recent concern, especially among young population. The inclusion of tobacco in the betel quid adds significantly to the carcinogenicity.

Alcohol Use

Epidemiological studies suggests that drinking alcoholic beverages multiplies the risk of oral carcinoma 2-6 folds and it itself is an independent risk factor (IARC 2010), with risk rising with quantity consumed. The risk varies with population and individual and subsite in the oral cavity. The combined use of alcohol and tobacco has a synergistic effect on oral carcinoma risk. The various pathways by which alcohol may exert carcinogenic influence such as topical

exposure leading to a direct effect on cell membranes, altered cell permeability, difference in enzymes that metabolize alcohol, and/or systemic effects, such as nutritional deficiency, immunological deficiency, and altered liver function. A recent review couldn't find an association between the use of mouthwash composed of alcohol and oral carcinoma risk, or any significant trend in risk with increasing daily usage of mouthwash.

Polymorphisms in alcohol-metabolizing enzymes also adds on to the risk. Individuals with the rapid-metabolizing version (allele) of alcohol dehydrogenase have a greater risk of developing oral carcinoma in the presence of alcoholic beverage consumption than those with the delayed-metabolizing forms; this higher risk establishes the role of acetaldehyde as the carcinogen involved.[18]

Poor Nutrition

Adequate consumption of fruits and vegetables is associated with a significant reduction of 40–50 % in the risk of oral carcinoma.[16] In high income countries (HICs), selected aspects of diet—such as lack of vegetables and fruits—may account for 15–20% of oral carcinomas. This proportion is likely to be higher in low-middle income countries (LMICs). Chemoprevention studies couldn't established a preventive effect of retinoid and carotenoid dietary supplements.[17]

Genetic Factors

Most carcinogens are metabolized via the cytochrome p450 system in the liver. In case this system is defective by virtue of inheriting a particular variant of the gene, the risk of many carcinomas is augmented. This risk is particularly important with oral and other head and neck carcinomas, even though the relative risks are modest at 1.5 or lower.

Mate Drinking

Mate, a leaf infusion that is generally drunk multiple times a day on daily basis in parts of South America—usually very hot is considered to raise the risk of oral carcinoma by a small amount.

Viruses

HPV have been identified in association with various human cancers. Amongst all the HPV related carcinomas, HPV associated oral cavity carcinomas has risen exponentially in men

under the past 50 years period. In the western world like US, the rate of HPV related head and neck carcinoma is near to 70%. There as nearly 140 subtypes of HPV categorized into high risk oncogenic types and low risk non oncogenic types. HPV 16 being high risk variant constitutes most of the head and neck cancers upto 80% globally. Another variant of HPV, HPV 18 is also a high malignant variant is associated in 34% patients of oral cavity carcinoma.[58,59] The HPV associated oral carcinoma has much better prognostic value than those HPV negative carcinoma with different clinical and biological characteristics. HPV associated HNC SCC have infrequent association with p53 mutations. [60] Cases are documented in those patients who have few oral sexual partners upto 40% cases but its till unclear for the fact that HPV associated oral carcinoma is more in cases of men rather than women. HPV may regulate the process of carcinogenesis in some tobacco-induced and alcohol-induced oral and oropharyngeal carcinomas, and it may act as the primary oncogenic agent by inducing carcinogenesis among nonsmokers. The pathogenesis of HPV associated oral carcinoma is more or like similar to cervical carcinoma.

Chronic Trauma

It seems clear that chronic local trauma due to sharp teeth, restorations, or dentures, increases the oral carcinoma risk, even though this higher risk generally occurs only in the presence of the other local risk factors. It has been suggested persistent mechanical irritation leads to DNA damage and may gradually result in cancer formation. It has been proven to have increased activity of poly-ADP-ribose polymerase in case with chronic trauma due to broken tooth, caries, dentures etc. [61] Most commonest site of carcinoma in oral cavity due to mechanical trauma is in the lateral aspect of the tongue.[62]

Most of the metal dentures, filled or decayed tooth are having association with oral carcinoma with more association with duration of the above mentioned causative factors. Chronic mucosal insult happens in those with sharp or broken tooth over a period of time in their location on alveolar arch.[63]

Figure 11 Carcinoma of lateral aspect of tongue

Figure 12 Decayed tooth causing mechanical trauma

PATHOLOGY

Squamous cell carcinomas (SCC) constitute not less than 90% of all oral carcinoma. Other malignant tumors can develop from the epithelium, connective tissue, minor salivary glands, lymphoid tissue, and melanocytes or metastasis from a distant primary Tumor.

Squamous cell carcinoma originates from the dysplastic surface epithelium. Multiple varients of squamous cell carcinoma are in existence as;

1. **Adenoid squamous cell carcinoma**: Microscopically, the tumor designed as a lobular growth pattern of keratinizing SCC that shows central regions of rounded spaces.
2. **Verrucous carcinoma**: low grade locally aggressive tumor with histologically broad based and invasive and infolding epithelium that is deficient with malignant features.

Superficial section resembles verruca with hyperkeratosis, parakaertosis and acanthosis.

3. **Spindle cell carcinoma:** It histologically exhibitis areas of SCC and spindle cells.
4. **Basaloid SCC:** They exhibit conventional SCC features with additional follicular or lobular pattern of invasion.
5. **Papillary SCC:** Uncommon. More of benign fibrovascular cores with with overlying squamous cell epithelium. More commonly seen in HPV infections
6. **Mucin producing SCC:** More aggressive variant with wild clinical course than most of the cutaneous SCC
7. **Lymphoepithelioma:** Lymphoepithelial variant of SCC, develops with distinctive intermingling of undifferentiated carcinoma cells with prominent lymphoid stroma.

Other types of carcinomas that can arise in oral cavity are;

1) **Salivary gland adenomas:**
   a) Pleomorphic adenoma
   b) Myoepithelioma
   c) Basal cell carcinoma
   d) Canalicular adenoma
   e) Duct pappiloma
   f) Cystadenoma
2) **Salivary gland carcinomas:**
   a) Acini cell carcinoma
   b) Mucoepidermoid carcinoma
   c) Adenoid cystic carcinoma
   d) Cystadenocarcinoma
   e) Mucinous adenocarcinoma
   f) Salivary duct carcinoma
   g) Clear cell carcinoma
3) **Soft tissue sarcomas:**
   a) Kaposi sarcoma
   b) Lymphangioma
   c) Focal oral mucionsis
4) **Hematolymphoid tumors**
   a) Diffuse large B-cell lymphoma

b) Mantle cell lymphoma
c) Follicular lymphoma
d) T cell lymphoma
e) Burkitts lymphoma

5) **Mucosal malignant melanomas:** Mucosal melanoma (MM) is a rare melanoma subtype that arises from melanocytes within sun-protected mucous membranes. When compared to cutaneous melanoma (CM), MM has worse prognosis and lacks effective management options. Causative factor being the same as tobacco, alcohol in case of oral mucosal melanoma patients. Occurs generally in the hard palate and maxillary gingiva where there is keratinized mucosa in abundance. It shows various colours from black to red or white alongwith asymmetric and irregular morphology. Compared to cutaneous melanoma, mucosal melanoma doesn't have clear cut classification but those with histologic patterns are still controversial. [57]

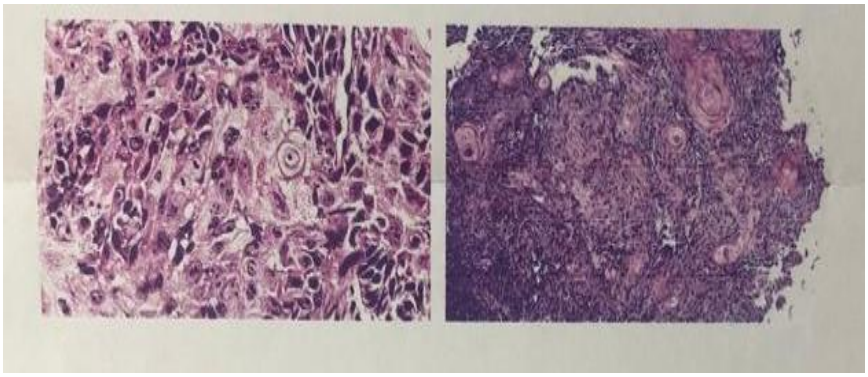

Figure 13 Infiltrating Squamous cell carcinoma

Many a number of premalignant lesions have been associated with development of SCC. Upon which common premalignant lesions including leukoplakia, erythroplakia, oral lichen planus, and oral submucous fibrosis have varying potency for malignant transformation. The WHO (2005) classifies premalignant lesions according to their degree of dysplasia as mild, moderate, severe, and carcinoma in situ.

Erythroplakia is a bright red velvety patchy lesion which cannot be characterized clinicopathologically as being caused by any other clinical cause. Surgical excision is recommended as these lesions have higher malignant transformation compared to leukoplakia and are commonly in association with dysplasia and carcinoma in situ.

Figure 14 Leukoplakia

Leukoplakia is defined as a "white patch or plaque that cannot be characterized clinicopathologically as any other disease". It is usually associated with smoking and alcohol use. The prevalence of leukoplakia worldwide is approximately 2%. Dysplastic changes are present in only 2–5% of patients. The annual rate of malignant transformation in patients with leukoplakia is 1%. Risk factors for malignant transformation such as presence of dysplasia, female gender, longer duration of leukoplakia, site on the tongue or floor of mouth, leukoplakia in non-smokers, size more than 2cm, and non-homogeneous type. In addition to lifestyle changes to avoid tobacco and alcohol use, excision stays the only definitive modality for accurate diagnosis and treatment.

Non-squamous cell carcinomas of the oral cavity are less frequent. Minor salivary gland carcinomas represent not more than 5% of the oral cavity carcinomas. They frequently develop on the hard palate [60%], lips [25%] and buccal mucosa [15%]. Mucoepidermoid carcinoma is the commonest type [54%], followed by low-grade adenocarcinoma [17%], and adenoid cystic carcinoma [15%].[13]

Mucosal melanomas are very rare but generally present as locally aggressive Tumors, usually of the hard palate and gingiva. Bony Tumors like osteosarcoma of the mandible or maxilla and odontogenic Tumors such as ameloblastoma can be present with in the oral cavity and may be mistaken for a mucosal lesion if there is any surface ulceration.

Figure 15 Sublingual salivary gland neoplasm

CLINICAL PRESENTATION AND EVALUATION

Despite simple easy self-examination and physical examination, patients often present and gets diagnosed with advanced stage disease. General presentation of patients to doctors are with ulcer in the oral cavity which bleeds on touch. Edges will be irregular and everted with cauliflower like growth. The second commonest presentation was with swellings in the cheek or to the submandibular region which in later stags can erode the skin and the can even create fistula also. When the growth infiltrates into the masticatory muscles, there will be e associated trismus and difficulty in mastication and deglutition.

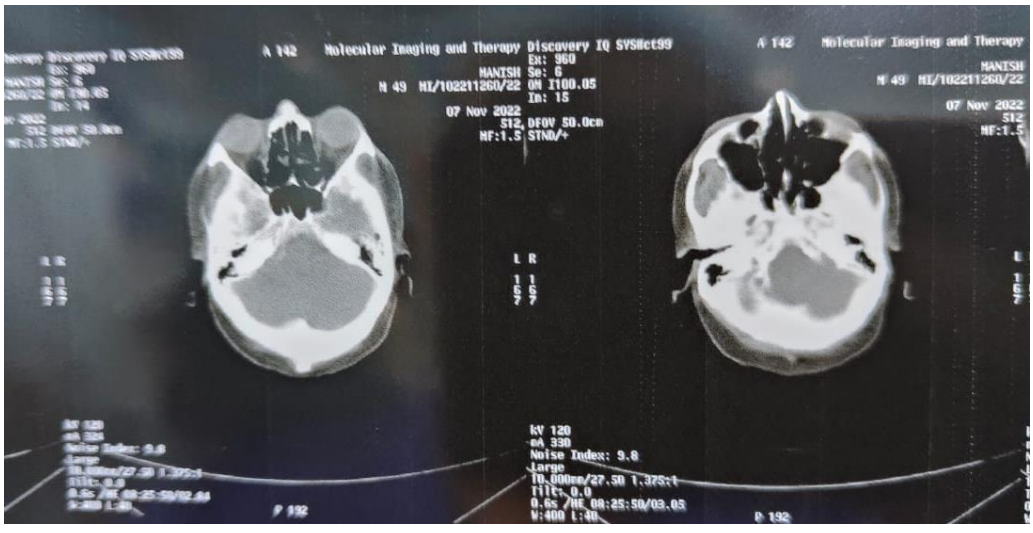

Figure 16 CECT of Head and neck showing tumor in the right buccal mucosa

Most of these are the commonest presentation and these patients will present to OPDs delayed. A detailed head and neck exam is mandatory in patients with suspected oral cavity carcinoma. Visual inspection and palpation allow a precise impression of the extent of the disease, the third dimension of Tumor, the bone invasion, or skin breakdown. Adequate documentation with drawings and photographic records of the Tumor are helpful in staging, decision-making and eventual follow up.

The clinical TNM stage should be made at first encounter and modified as evaluation progresses. The initial workup consists of diagnosis by biopsy whether being punch biopsy or core needle biopsy. Accessible lesions may be adequately biopsied in OPD basis using punch forceps, core needle or fine-needle aspiration. Some patients require examination under general anesthesia (EUA) so as to access posteriorly situated lesions, or to complete a physical exam that are limited by pain and trismus. Radiographic imaging is critical for assessment of the relation of the tumor to adjacent bone and for assessing regional lymph nodes. CT scan is the investigation of choice for assessment of bone and neck nodes, especially early cortical involvement and extracapsular nodal infiltration. MRI provides add on extra information about soft tissue extent and perineural invasion and also aids for evaluating the extent of medullary bone infiltration as adult marrow is generally replaced by fat.

Most patients with oral carcinoma are having less risk for distant metastases and therefore the importance of PET scan in initial assessment is no yet standardized. However, a preoperative PET scan may be useful as a baseline if adjuvant treatment is being planned and a PET scan will be useful for radiation therapy planning. Patients with locally advanced tumors necessitates appropriate multidisciplinary approach with the plastic reconstructive surgeon, medical specialists for presurgical optimization, dental professionals, speech and swallowing pathologists, and behavioral therapists for smoking cessation and other lifestyle modifications.

The TNM system is the most accepted prognostic criteria due to its fairly simple design and user-friendliness. The clinical staging of the oral cavity carcinomas consists of primary tumor characteristics, the neck, and assessment for distant metastases. This data allows TNM stage grouping for the tumor. The basic elements in staging of the primary site are the size of Tumor and infiltration to deeper structures. Advanced disease is defined by infiltration into structures like medullary bone, deep muscle of the tongue, maxillary sinus, and skin for T4a disease, or masticator space, pterygoid plates, or skull base and/or encasement of the internal carotid artery for T4b stage. Lymphatic spread into the neck usually occurs in a step-wise, orderly and

predictable manner. The lymph node echelons of the neck are defined using the terminologies which are standardized by the American Head and Neck Society Guidelines.

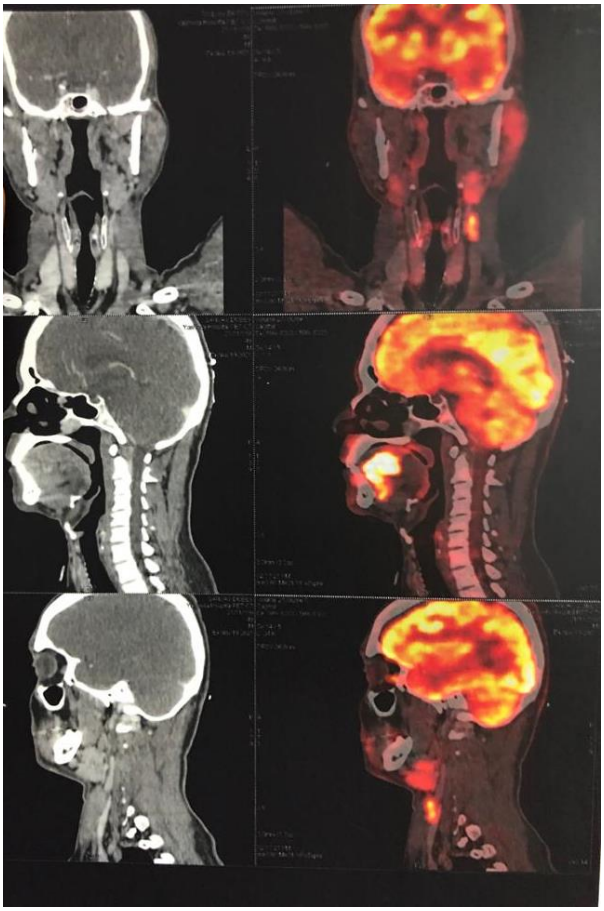

Figure 17 PET scan of Left Buccal mucosa carcinoma with reactive cervical lymph nodes

Knowledge of the patterns of nodal metastatic spread has practical importance in the design of neck dissection for patients with oral carcinoma. The patient with a clinically negative neck is at highest risk of occult metastasis to levels I–III. Skip metastases to level IV also do occur, especially in carcinoma of the anterior 2/3rd tongue. Metastases to level V are extremely rare (1%) even in patients with clinically positive neck. Oral tongue Tumors have the highest tendancy of all oral carcinomas for metastasis to the neck, and Tumor thickness is a major predictive factor of risk of nodal metastasis.[14]

Survival

In the United States, five-year survival improved by more than 11 percentage points between 1992 and 2006 and is currently approximately 65 %. In Europe, it comes close to 50 %. In India, five-year survival is not more than 35 %. In China, the Republic of Korea, Pakistan,

Singapore, and Thailand, it ranges between 32 and 54 %. Overall, the five-year survival for early, localized carcinomas is above 80% and falls to less than 20% when cervical lymph nodes are positive.

Oral Carcinoma: Risk Factors and Prevention

The major causes of oral carcinoma worldwide remain tobacco in its various forms, consumption of alcohol, and, increasing infections with certain types of viruses like HPV. Even though the relative contribution of risk factors differs from population to population, oral carcinoma is predominantly a disease of poor people as in those with low socio-economic status. Prevention of this treacherous disease can come from basic changes in socio-economic status, as well as from actions to reduce the demand, production, marketing, and consumption of tobacco products and alcohol. A healthy diet, adequate oral and sexual hygiene, and awareness of the symptoms and signs of disease are important. Success relies on political will, intersectoral intervention, and culturally sensitive public health messages disseminated through educational campaigns, pamphlets regarding the same and mass media initiatives.

Oral Carcinoma: Natural History

Oral carcinoma has a very long preclinical phase that is composed of well-documented precancerous lesions. The precancerous lesions such as homogeneous leukoplakia, nonhomogeneous leukoplakia, verrucous leukoplakia, erythroplakia, OSMF, lichen planus, and chronic traumatic ulcers. The estimated yearly frequency of malignant transformation of oral precancerouus lesions ranges from 0.13 % to 2.2 %.[19]

Early preclinical invasive carcinomas present as painless small ulcers, nodular lesions, or growths. These changes can be easily visualised and are clinically detectable through careful examination with inspection and palpation of the oral mucosa. Early oral carcinomas less than 4 cm that have not spread to the regional lymph nodes can be effectively treated and cured with surgery or radiotherapy alone, with no functional or aesthetic defects, resulting in 5-year survival rates more than 80%.

Advanced cases are those that are clinically challenging for even primary resection as well as for reconstruction. Many a number of cases presenting with advanced cases are planned for primary Tumor excision along with aesthetic reconstruction for both functional and cosmetic advantage followed by chemoradiation to prevent Tumor recurrence. Local recurrence Is one major postop complication which the patient present within a period of 2-5 years. If the Tumor

seems unresectable, as I cases of skull base extensions, patient will be put in for palliative case and so does if the patient have large Tumors occupying major spaces in the face and neck. These patients will be put for palliative chemotherapy and other supportive treatment like pain relief and nutrition for the rest of their life time.

Oral Carcinoma Screening: Accuracy, Efficacy, and Potential Harms

Even when an affordable, acceptable, easy to perform, precise, and effective screening test for oral carcinoma is prevailing in high-risk countries, a decision to introduce population-based screening should consider the level of health service development and available resources to cope up with the increased management demand that screening generates. The target population for oral carcinoma screening include those aged 30 years and older who consume tobacco and/or alcohol.

Visual screening of the oral cavity has been widely practiced for its feasibility, safety, acceptability, accuracy to diagnose oral precancerous lesions and carcinoma, and efficacy and cost-effectiveness in decreasing oral carcinoma mortality.[19] Visual screening involves systematic visual and physical examination of the intraoral mucosa with the help of bright light for signs of oral potentially malignant disorders (OPMDs), as well as early oral carcinoma, followed by careful inspection and digital palpation of the neck for any lymphadenopathy. It is a examiner-dependent, subjective test. Accordingly, its performance in noticing lesions varies among those who conducts it. Thorough knowledge of the anatomy of oral cavity, the natural history of oral carcinogenesis, and the clinico-pathological features of the OPMDs and preclinical carcinomas are important requisites for efficient examiners of oral visual screening.

The potential flaw of oral visual screening may include further diagnostic investigations, such as incisional or excisional biopsy. Anxiety associated with false-positive screening tests. Diagnosing and treatment of biologically insignificant conditions that may have least impact on oral carcinoma incidence and false assurance from false-negative tests.

Visual Screening by Health Care Personnel

A multidisciplinary group of health care personnel consisting of dentists, general practitioners, oncologists, surgeons, nurses, and auxiliary health workers—may facilitate oral visual screening after training. Sensitivity ranges from 40 % to 93 %, and specificity ranges from 50 % to 99 % for diagnosing precancerous lesions and early asymptomatic oral carcinomas .[19,20]

A significant decline of 34 % in oral carcinoma death among a high-risk group of tobacco or alcohol consumers following three rounds of oral visual screening has been identified in a cluster-randomized controlled trial in India. A 15-year follow-up found sustained reduction in oral carcinoma death with larger decline in those adhering to repeated screening rounds. There was a 38 % decline in oral carcinoma incidence (95 % confidence interval [CI] 8–59 %), and an 81 % decline in oral carcinoma death (95 % CI 69–89 %) in tobacco and/or alcohol consumers who were screened 4 times. The studies were the source for the conclusions of the current Cochrane Collaboration Review and an American Dental Association (ADA) expert panel review recommends the clinicians to look for signs of precancerous lesions or early-stage carcinomas while performing routine visual and tactile screening in all subjects, usually in those who use tobacco or alcohol or both; the panel also confirmed that the life-saving advantages for subjects with curable lesions were more important than the potent risks incurred by those with benign or nonprogressive lesions. The Cochrane Review decided that evidence suggests that a visual examination as part of a population-based screening program reduces the death rate of oral carcinoma in high-risk individuals alongwith, it could result in diagnoses of oral carcinoma at an earlier stage of disease and betterment in survival rates across the whole population. [19,20]

The U.S. Preventive Services Task Force issued a draft recommendation Statement, which mentioned that for adults age 18 years or older found in primary care settings, the current evidence is inconclusive to assess the balance of advantages and disadvantages of screening for oral carcinoma in asymptomatic adults. However, this statement oversees the benefits of early diagnosis of oral carcinomas among chronic users of tobacco or alcohol or both, as well as those benign conditions whose early diagnosis may improve oral health. Discouraging oral visual examination in primary care is clearly not in the line of interest of oral carcinoma control and improving oral health.

Self-Examination and Other Screening Methods

While oral self-examination using a mirror has been assessed as a screening test in some studies, whether it could lead to decline in oral carcinoma death is not known. There is a lack of evidence to suggest the routine use of other oral screening tests, such as toluidine blue staining, chemiluminescence, tissue fluorescence imaging, tissue fluorescent spectroscopy, and salivary examination and cytology for initial screening of oral carcinoma.

Despite the increased risk of oral carcinoma in the Indian subcontinent, no national or regional screening programs exist in the country other than statutory warning for tobacco and alcohol products. The only large-scale, ongoing, national oral carcinoma screening programs are in countries like Cuba and Taiwan, China.

The Cuban program has been in existence since late 1984. An evaluation completed in 1994 mentioned that 12–26 % of the target population has been screened yearly, but less than 30 % of screen-positive individuals complied with referrals. The program was reorganized in 1996, with the target age increased from 15 years to 35 years, screening intervals raised from 1 to 3 years, and the referral system refurnished. No further formal analysis has been done, but there has been no decline in oral carcinoma incidence or death rates in Cuba over the past few decades. The outcomes from the Cuban program emphasize that screening programs with out efficient organization and resources are not an effective method of limited resources.

Oral carcinoma screening was started in Taiwan, China, in 2004, aiming those age 18 years and older who were smokers or betel nut chewers. The target population for oral carcinoma screening was updated in 2010 to cover smokers or chewers age 30 years and more. The screening program has been successful in identifying almost half of the oral carcinomas diagnosed in stages I and II, with a declining trend in oral carcinoma death rates.[20]

Oral Carcinoma: Early Clinical Diagnosis and Staging

Primary care dental and general practitioners should play an important role in referring patients to carcinoma treatment facilities for early diagnosis and management. Improving the skills of these primary care doctors is needed to improving prospects for early diagnosis, particularly among patients who use tobacco or alcohol in any kind. Routine biopsy in those clinically presenting with signs of precancerous lesions can lead to early diagnosis of underlying invasive oral carcinoma. In addition to history, physical examination, and biopsy, a simultaneous evaluation of the upper aerodigestive tract is mandatory because patients with oral carcinoma have a higher risk of carcinomas developing in other head and neck sites and in the lungs.

Once a diagnosis of oral carcinoma is made, staging assessment is finalised and management is planned. The Union for International Carcinoma Control Tumor, Nodes, Metastasis (TNM) staging system is generally used for staging oral carcinoma. T denotes the size and extent of local spread of the primary tumor, N denotes the spread to the regional lymph nodes in the neck, and M denotes the spread to distant organs. The TNM categorization is further grouped

into stages 0 through IV, which indicates increasing severity of disease and declining survival rate.[13]

Oral carcinoma staging includes assessing the clinical spread of disease through physical examination, biopsies, and radiological investigations, like X-rays of the mandible, maxillary sinuses, and chest, computerized tomography (CT) scans, magnetic resonance imaging (MRI) and positron emission tomography (PET) imaging, based on what resources are offered. Advanced imaging techniques such as CT, MRI, and PET may be helpful in more accurately assessing local spread, such as infiltration into muscles, bone, and cartilage, and lymph node metastases and also in planning treatment, but these investigations are rarely feasible and available in LMICs.[19]

AJCC 8th grading of Oral carcinoma & staging

Table 1 Primary tumor (T) definition oropharyngeal cancers.

TX	Primary tumor cannot be assessed
Tis	Carcinoma *in situ*
T1	Tumor ≤ 2 cm and DOI ≤ 5 mm
T2	Tumor ≤ 2 cm, DOI > 5 mm and ≤ 10 mm ***or*** tumor > 2 cm and ≤ 4 cm and DOI ≤ 10 mm
T3	Tumor > 4 cm ***or*** any tumor with DOI > 10 mm
T4 **T4a** **T4b**	 Tumor invades adjacent structures only (e.g., through cortical bone of mandible or maxilla, or involves the maxillary sinus or skin of the face) Tumor invades masticator space, pterygoid plates, or skull base and/or encases the internal carotid artery

Table 2 Primary tumor (T) definition for HPV-related (p16-positive) oropharyngeal cancers.

T0	No tumor identified, but p16+ cervical node(s) involvement
Tis	Carcinoma *in situ*
T1	Tumor ≤ 2 cm
T2	Tumor > 2 cm and ≤ 4 cm
T3	Tumor > 4 cm or extension to lingual surface of the epiglottis
T4	Moderately advanced local disease; tumor invades larynx, extrinsic muscle of tongue, medial pterygoid, hard palate, or mandible or beyond

Table 3 Clinical assessment of regional lymph nodes (cN) in HPV negative oral cancers

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral lymph node, ≤ 3 cm and ENE-
N2 **N2a** **N2b** **N2c**	Metastasis in a single ipsilateral lymph node > 3 cm and ≤ 6 cm and ENE- ; ***or*** metastases in multiple ipsilateral lymph nodes, ≤ 6 cm and ENE-; ***or*** in bilateral or contralateral lymph nodes, ≤ 6 cm and ENE- Metastasis in a single ipsilateral lymph node > 3 cm and ≤ 6 cm and ENE- Metastases in multiple ipsilateral lymph nodes, ≤ 6 cm and ENE- Metastases in bilateral or contralateral lymph nodes, ≤ 6 cm and ENE-
N3 **N3a** **N3b**	 Metastasis in a lymph node > 6 cm and ENE-; ***or*** metastasis in any lymph node(s) with ENE+ clinically Metastasis in a lymph node > 6 cm and ENE- Metastasis in any lymph node(s) with ENE+ clinically

Table 4 Clinical assessment of regional lymph nodes (cN) in HPV-related (p16-positive) oropharyngeal cancers.

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	One or more ipsilateral lymph nodes ≤ 6 cm
N2	Contralateral or bilateral lymph nodes ≤ 6 cm
N3	Lymph node(s) > 6 cm

Table 5 Pathological assessment of regional lymph nodes (pN) in HPV negative oral cancers

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral lymph node, ≤ 3 cm and ENE-
N2 **N2a** **N2b** **N2c**	Metastasis in a single ipsilateral lymph node, ≤ 3 cm and ENE+; ***or*** metastasis in a single ipsilateral lymph node > 3 cm and ≤ 6 cm and ENE-; ***or*** metastases in multiple ipsilateral lymph nodes, ≤ 6 cm and ENE-; ***or*** in bilateral or contralateral lymph nodes, ≤ 6 cm and ENE- Metastasis in a single ipsilateral lymph node, ≤ 3 cm and ENE+; ***or*** metastasis in a single ipsilateral lymph node > 3 cm and ≤ 6 cm and ENE- Metastases in multiple ipsilateral lymph nodes, ≤ 6 cm and ENE- Metastases in bilateral or contralateral lymph nodes, ≤ 6 cm and ENE-

N3 **N3a** **N3b**	Metastasis in a lymph node > 6 cm and ENE-; ***or*** metastasis in a single ipsilateral node larger than 3 cm in greatest dimension and ENE+; ***or*** multiple ipsilateral, contralateral, or bilateral nodes, any with ENE+; ***or*** a single contralateral node of any size and ENE+ Metastasis in a lymph node > 6 cm and ENE- Metastasis in a single ipsilateral node larger than 3 cm in greatest dimension and ENE+; ***or*** multiple ipsilateral, contralateral, or bilateral nodes, any with ENE+; ***or*** a single contralateral node of any size and ENE+

Table 6 Pathological assessment of regional lymph nodes (pN) in HPV-related (p16-positive) oropharyngeal cancers.

pNX	Regional lymph nodes cannot be assessed
pN0	No regional lymph node metastasis
pN1	Metastasis in 4 or fewer lymph nodes
pN2	Metastases in more than 4 lymph node

Table 7 AJCC prognostic clinical stage groups for HPV-related (p16-positive) oropharyngeal cancers.

I	T0N1M0, T1N0M0, T1N1M0, T2N0M0, or T2N1M0
II	T0N2M0, T1N2M0, T2N2M0, T3N0M0, T3N1M0, or T3N2M0
III	T0N3M0, T1N3M0, T2N3M0, T3N3M0, T4N0M0, T4N1M0, T4N2M0, or T4N3M0
IV	Any T, any N, and M1

Table 8 AJCC prognostic pathological stage groups for HPV-related (p16-positive) oropharyngeal cancers.

I	T0N1M0, T1N0M0, T1N1M0, T2N0M0, or T2N1M0
II	T0N2M0, T1N2M0, T2N2M0, T3N0M0, T3N1M0, T4N0M0, or T4N1M0
III	T3N2M0, or T4N2M0
IV	Any T, any N, and M1

ORAL CARCINOMA: MANAGEMENT

Surgical resection is the primary treatment of choice for SCCOC. Surgical resection favours precise pathologic staging, with information regarding the status of margins, Tumor spread and histopathologic features which can then be utilized to inform subsequent treatment based upon valuation of risk upon benefit. Adjuvant radiotherapy ± chemotherapy is given to those with locoregionally advanced tumors. A multidisciplinary approach is absolutely essential to make

sure a desirable outcome. Multiple factors are considered in choosing treatment for an individual patient. The risk of treatment-related complications should be evaluated based on physiological age, comorbid disease (eg. cardiopulmonary status), lifestyle (smoking or alcohol), surgical resectability, and patient desires.[25]

SURGICAL MANAGEMENT

Primary treatment of choice for carcinoma of oral cavity is surgical management with post op chemoradiation as respect to the staging of the Tumor. As it is having one of the complex anatomies with close proximity of vital structures in the neck and face, access to the Tumor and nodes are challenging. Broad principles of surgical management will be dealt and these include the access to the oral cavity, management of the mandible, management of neck nodes, and plastic reconstruction of oral cavity surgical defects.The transoral approach is usually done for premalignant lesions and small, superficial Tumors of the anterior floor of mouth, alveolus and tongue. For posteriorly located Tumors demands a more invasice approach or if there are limitations due to trismus or inadequate surgical exposure The lip-splitting paramedian mandibulotomy approach is done for larger posteriorly situated Tumors of the tongue. The upper cheek flap and midfacial degloving approaches are helpful for gaining access to the maxilla.[30]

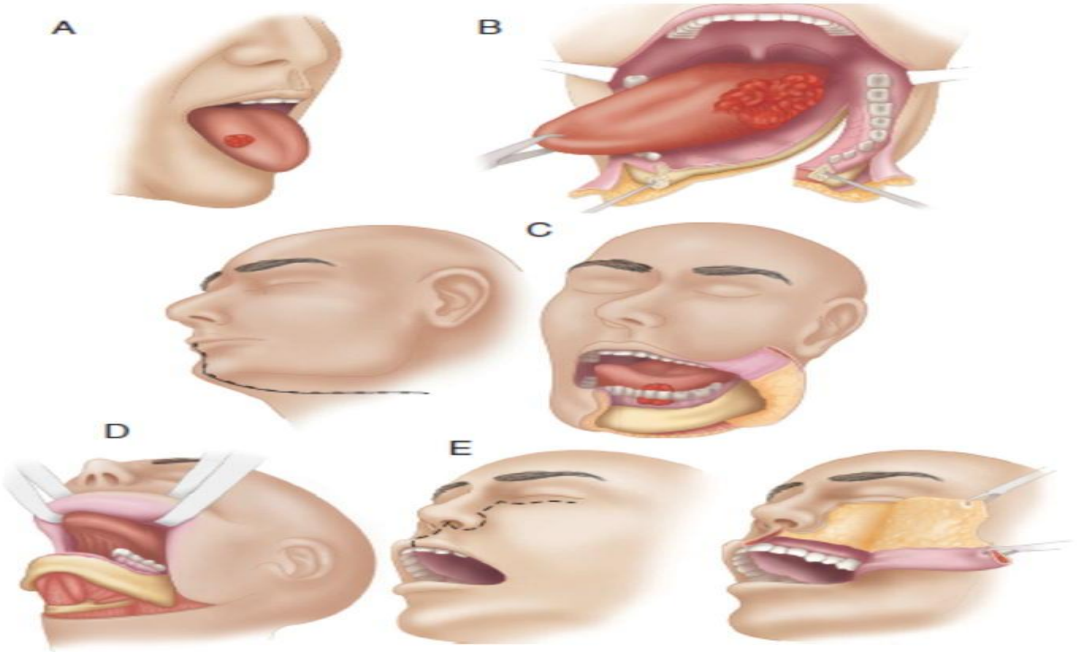

Figure 18 Approach to oral cavity

MANAGEMENT OF THE MANDIBLE

Mandibular invasion can occur initialy in Tumors of the floor of the mouth, the ventral surface of the oral tongue and the gingivobuccal sulcus. Tumors invade the mandible via the dental sockets in the dentate mandible, and via the dental pores of the alveolar process in the edentulous mandible.[35]

Initial cortical invasion of the mandible is difficult to evaluate with plain radiography, or orthopantomograms but CT scans are more sensitive. On a management basis, Tumors that are in near to the mandibular cortex requiring consideration for marginal mandibulectomy in order to achieve a sufficient margin of resection even with radiographically evident early cortical invasion. The role of marginal resection might be restricted in patients with reduced vertical height of the body of the mandible because of the higher risk of early involvement of the body of mandible and the tendency for pathologic fracture if a marginal resection is performed. Adequate Tumor clearance in edentulous patients may therefore demands a segmental mandibulectomy.

Figure 19Left hemimandibulectomy specimen

MANAGEMENT OF THE NECK

60% of patients with early stage oral carcinoma will present with a clinically negative neck [cN0]. nearly 20–30% will have microscopically apparent nodal metastasis on histopathlogic examination after elective neck dissection (END). The risk of nodal metastasis is related to various factors. Cervical lymph node metastasis is the single most significant prognostic factor in oral carcinoma. Survival chances are low by 50% when equated to those with similar primary Tumors with negative neck metastases. SCC of the oral tongue and the floor of the mouth are more highly likely to metastasize to the neck, and these patients should be advised END, even for early-stage Tumors, if they are larger than about 4mm. The hard palate and the upper gum have a relatively lower rate of occult nodal metastasis and END may not be suggested.

Figure 20 Post MRND for Buccal Carcinoma with reactive lymphnodes in level 1B,2A

Sentinel node biopsy is an alternative technique to END for staging the cN0 neck in early stage (T1–2) SCCOC. The technique was first studied in 2001 by 50 and has been evaluated in several single institutional studies as well as ac couple of prospective multicenter trials, one in Europe and the other in the US. The procedure is technically challenging and effective identification of sentinel nodes and noticing occult metastasis be subject to on expertise and experience. Therefore, it should be assumed only in centers with the essential proficiency and the suitable volume of cases.[21]

In patients with clinically or radiographically positive neck nodes, a therapeutic comprehensive neck dissection is directed. It includes dissection of levels I to V. The need to detriment other structures such as the spinal accessory nerve, sternocleidomastoid muscle, or internal jugular vein hang on the location of the metastasis and its features. The commonest type of comprehensive neck dissection is the modified radical neck dissection, MRND Type 1. Radical neck dissection is seldom performed except if there is direct intrusion of the relevant structures by gross extranodal extension of disease.

In a patient with a clinically negative neck, the risk of occult metastasis is mostly to levels I to III. Potential negotiation of levels IV and V is very rare. Due to these reasons, a supraomohyoid neck dissection (SOHND) is usually satisfactory to stage the cN0 neck. In patients with primary oral tongue SCCOC dissection of level IV may be directed because of the prospect of skip metastasis. For patient with positive nodes on END, neck recurrence is detected in 10–24%. Suitably selected patients advantage from postoperative radiation therapy. For cN0 patients who are proven pathologically N0, failure rates of not more than 10% have been testified.

RECONSTRUCTIVE SURGERY

Restoration of aesthetic and functionality after ablative carcinoma surgery is the final goal of treatment and is achieved by selecting the suitable reconstructive procedure. Surgical defects after resection of early stage Tumors can generally be reconstructed with primary closure or the use of skin graft or skin substitutes. Reconstruction of larger and complex defects that result from resection of advanced Tumors requires an expert plastic reconstructive surgeon. Microvascular free tissue transfer is the procdure of choice. For example, in patients with soft tissue defects of the oral tongue, floor of mouth and retromolar trigone, the free radial forearm flap results in exceptional functional results. In addition to the soft tissue cover, free flaps are also a dependable source for bone reconstruction.

Figure 21 Mandibular reconstruction with radial forearm osteocutaneous flap

The fibula free flap is presently the workhorse in reconstruction of defects after segmental mandibulectomy. Other composite microvascular flaps comprise the radial forearm osteocutaneous flap, iliac crest and scapula free flaps. Numerous studies have demonstrated the reliability and low morbidity of microvascular free flap reconstruction techniques. The facility reliably to reconstruct large surgical defects has contributed to enhanced oncologic outcomes in patients with locally advanced carcinomas by enabling supplementary complete resections. Pedicled myocutaneous flaps such as the pectoralis major, latissimus dorsi or trapezius flaps are dependable alternatives if surgical expertise is not accessible or if the patient is not an ideal candidate for microvascular reconstruction.

Figure 22 PMMC flap reconstruction underway for Carcinoma of Buccal Mucosa

ADJUVANT TREATMENT

Adjuvant postoperative treatment is designated in those patients with high risk of locoregional recurrence. This comprises patients with large primary Tumors (pT3 or pT4), bulky nodal disease (pN2 or pN3), metastases to nodal levels IV or V, positive surgical margins [R1 and R2 resection], lymphovascular invasion, perineural invasion, and extracapsular invasion. External beam radiation therapy has been the outdated modality for postoperative adjuvant treatment and doses of Gy result in acceptable locoregional control [22]. Multiple clinical trials have suggested that administration of cisplatin chemotherapy concurrently with postoperative radiotherapy favours locoregional control and survival (versus radiotherapy alone) in head and neck carcinoma patients with extracapsular invasion and /or positive surgical margins. However, concurrent chemoradiation can end up in noteworthy morbidity and is best used at centers where appropriate expertise and set-up is available.

TREATMENT OF EARLY-STAGE ORAL CARCINOMA [STAGES I AND II]

Surgery and radiotherapy are treatment of choice for early oral carcinoma, either as single modalities or in combination. The choice of treatment be subject to the location of the Tumor, aesthetic and functional outcomes, age of the patient, associated diseases, patient's preference, and the availability of expertise.

Most early-stage oral carcinomas can be locally excised or treated with radiotherapy, with minimal functional and physical morbidity. Elective neck dissection to remove lymph nodes may be indicated in selected cases, such as patients with stage I tongue carcinoma and stage II carcinomas at other oral sites, who may be at high risk of microscopic/occult but not clinically evident involvement of the neck nodes (N0)[23].

External beam radiotherapy and brachytherapy with radioactive sources implanted in the tumor either alone or in combination, is a substitute to surgery for early-stage oral carcinomas. Excellent results have been established following brachytherapy alone or in combination with external beam radiotherapy for small tumors. Deep infiltrative carcinomas have a high tendency to metastasize to regional lymph nodes; therefore, brachytherapy alone, which does not effectively treat regional lymph nodes, is not advised. Newer techniques, such as three-dimensional conformal radiotherapy and intensity modulated radiotherapy, can reduce the side effects of radiotherapy by delivering the radiation dose to the Tumor much more precisely and

accurately excluding healthy surrounding tissues. However, these treatments require far more advanced equipment and are more expensive than conventional radiotherapy.

TREATMENT OF LOCALLY ADVANCED TUMORS OF THE ORAL CAVITY (STAGES III AND IV)

Locally advanced tumors are aggressive, and locoregional treatment recurrence rates are high. A combination of treatment modalities integrating surgery, radiotherapy with or without chemotherapy, and planned and implemented by a multidisciplinary team is always recommended. Appropriate importance should be given to factors such as functional and aesthetic outcomes and the available expertise. Surgery followed by postoperative radiotherapy is the recommended modality for patients with deep infiltrative tumors and those with bone infiltration. Postoperative concurrent chemo-radiation has been shown to be superior to radiotherapy alone in those with positive surgical margins showing cancerous changes indicating incomplete excision of the tumor such as in R1 or R2 resection. The use of neoadjuvant chemotherapy prior to surgery may eliminate the need to remove the mandible—a major benefit—although it does not change the survival benefit.

Primary radiotherapy, with or without chemotherapy, is a reasonable choice for locally advanced tumors without bone infiltrates, especially for patients who have inaccessible disease, those who are medically unfit for surgery, or who are likely to have unacceptable functional and aesthetic outcomes with surgery. Incorporating chemotherapy with surgery or radiotherapy favours best outcome in younger patients who are in good general physical condition, increasing survival by nearly 5 % points at five years.

Side Effects of Radiotherapy

Side effects occurs while the procedure or immediately after radiotherapy—acute reactions—or months to years after treatment. Acute reactions are self-limiting and normally resolve with in 2 to 3 weeks. These reactions are due to the inflammation of tissues with in the radiotherapy treatment field. Alteration of taste, pain, difficulty in deglutition, mucosal ulceration of the oral cavity, bacterial and fungal infections, increased viscocity of saliva, discoloration and peeling of the overlying skin, hair loss with in the field of treatment, and edema of the skin are the major side effects. Maintenance of adequate oral hygiene, frequent cleaning of the oral cavity with soda-saline solution, analgesics, and control of infection are advised for conservative

management of these side effects. Good hydration, a high-calorie diet, and avoidance of spicy and hot food are suggested.

Late effects of radiation are associated with dose per fraction, total dose, and the type and volume of the tissue being irradiated. Late effects include loss of hair with in the irradiated area, xerostomia, thickening of the skin, dental caries, and, very rarely, necrosis of the mandible or maxillary bone.

Complications of Surgery

The general complications of oral surgery are infection, hematoma, skin necrosis, flap failure, and wound breakdown. Bone resorption, osteomyelitis, and salivary fistula can also occur. Complications are more common when neck dissection is also done. Fatal hemorrhage can occur if the carotid artery is exposed through the wound. Resection of the structures can interfere with aesthetic appearance and functions such as speech, swallowing, and airway. These complications can be minimalised with plastic reconstructive surgery and by good prosthetic rehabilitation.

Posttreatment Follow-Up

Patients with oral carcinoma are at risk for having loco-regional recurrences and second malignancies. After treatment completion, patients should be followed up at timely intervals to detect any signs of recurrence. Patients should be encouraged to be abstinent from tobacco and alcohol and to watch out for the signs and symptoms of recurrence.

Prognosis

Lymph node involvement and size of the tumor are the most significant prognostic factors. Data for the United States for 1975–2007 shows a five-year survival for all stages of oral carcinoma of 60.9 %, 82.5 % for early-stage disease, and 54.7% for locally advanced oral cavity carcinoma. The reported five-year overall survival rates for oral carcinoma for all stages combined from populations in LMICs such as China, Cuba, India, Pakistan, and Thailand ranged from 26 to 45%; for stages I and II, the survival rates ranged from 36 to 83%. The inferior survival rates in LMICs versus HICs suggests disparities in the availability, accessibility, and affordability of diagnostic and treatment facilities.

Economics of Preventing and Screening for Oral Carcinomas in LMICs

Cost-Effectiveness Assessments

There are only a few cost-effectiveness studies of oral carcinoma screening focus on LMICs; therefore, we include a broader spectrum of studies, including some from HICs. Although these studies may not be correlated resource-limited settings, they provide valuable insights into the potential cost-effectiveness of managements.

Primary Prevention

Interventions targeted on reducing or eliminating tobacco and alcohol consumption should be considered for implementation which shown to be more cost-effective. All the interventions presented are economical, even for LMICs. In the case of tobacco cessation, raising the price of tobacco products is the most cost-effective approach, with increasing cost-effectiveness ratios ranging from US$4 to US$34 per disability-adjusted life year. Alcohol control interventions tend to have much higher cost-effectiveness ratios; ban on advertising and reduced access range from US$367 to US$1,307. Combination strategies [including price hike, limited access, and advertisement bans] range between US$601 and US$1,704.

Jerjes W *et al* [24][2010] showed that the incidence of oral squamous cell carcinoma remains high. Oral and oro-pharyngeal carcinomas are the sixth commonest carcinoma in the world. Several clinicopathological parameters have been associated in prognosis, recurrence and survival, following oral squamous cell carcinoma. In this retrospective analysis, clinicopathological parameters of 115 T1/T2 OSCC were evaluated and compared to recurrence and mortality from tumor-related causes. The study proposal was approved by the Joint UCL/UCLH committees of the ethics for human research. The patients' data was entered onto proformas, which were checked by interval sampling. The fields consist of a range of clinical, operative and histopathological variables related to the clearance of the surgical margins. Data collection also included recurrence, cause of death, date of death and last clinic review as on follow up. Causes of death were grouped in 4 categories (1) death from locoregional spread, (2) death from distant metastasis, (3) death from pulmonary pneumonia, and (4) death from any non-tumor event that succumbs to cardiorespiratory failure. The patients population consists of 65 males and 50 females. Their mean age at the primary diagnosis of OSCC was 61.7 year([For male to female comparison). Most of the patients were Caucasians. Primary sites were mostly identified in the tongue, floor of mouth (FOM), buccal mucosa and

alveolus. Most of the identified OSCCs were lower stages (T1N0 and T2N0(For staging). all patients underwent primary resection ± neck dissection and reconstruction when indicated. Twenty-two patients had to avail adjuvant radiotherapy. Histopathological analysis revealed that half of the patients had moderately differentiated OSCC. pTNM slightly varied from the cTNM and showed that 70.4% of the patients had low-risk OSCC. Tumor clearance was finally achieved in 107 patients. Follow-up showed a 3-year survival of 74.8% and a 5-year survival of 72.2%. Recurrence was seen in 23 males and 20 females. The mean age of primary diagnosis of the recurrence group was 59.53 years [mean age]. Most common oral sites included the lateral border of tongue and floor of mouth [Subsite]. Recurrence had significant association with clinical N-stage disease. The surgical margins in this group were studied and found that 17 had non-cohesive infiltration, 30 had dysplasia at margin, 21 had vascular infiltration, 9 had neural invasion and 3 had bony infiltration. Severe dysplasia was found in 37 patients. Tumor clearance was accomplished in only 8 patients. The average depth of tumor invasion in the recurrence group was 7.6 mm. a significant finding was that 5/11 patients who died of distant metastasis had their primary tumor in the tongue. Nodal disease differentiation showed that 8/10 patients who died of locoregional metastasis and 8/11 patients who died from distant metastasis had clinical nodal involvement. When compared this to pathological nodal disease (pTNM) showed that 10/10 patients and 10/11 patients who died from locoregional and distant metastasis, respectively, had nodal disease. all patients who succumbed to death from locoregional and distant metastasis were found to have recurrence after the primary tumor resection. Squamous cell carcinoma of the oral cavity has a poor overall prognosis with a major tendency for recurrance at the primary site and infiltrates to involve the cervical lymph nodes. Several clinicopathological parameters can be taken to assess outcome, recurrence and overall survival.

Trotta BM *et al* [25][2011] found that the radiological findings in squamous cell carcinoma of the oral cavity and oropharynx vary widely, based on the site of origin of the primary Tumor and the extent of its infiltration to other regions. Knowledge of the complex anatomy of the oral cavity and oropharynx and the commonest routes through which SCC spreads from various anatomic sites, allows the radiologist to precisely determine the extent of disease and help surgeons to plan appropriate treatment. SCCs that arise in the oral cavity tend to behave differently than those that originate in the oropharynx, with the latter group producing a more aggressive growth. Furthermore, primary Tumors in some of the anatomic subsites within the oral cavity or oropharynx have a greater propensity to invade by direct extension along muscle,

bone, or neurovascular bundles or to be disseminated through lymphatic drainage pathways to regional or distant nodes. radiological findings of deep muscular, neurovascular, osseous, or nodal involvement are suggestive of an advanced stage of disease for which treatment modalities are limited.

Acharya S *et al* [26][2012] justified that substantial debate is in existence in the literature regarding the clinical course of young patients with oral squamous cell carcinoma (OSCC). Based on young patients with OSCC diagnosed at their institution, the clinicopathological features of OSCC in young patients were evaluated in order to determine if there were any defining characteristics in this population. all cases of OSCC diagnosed in their institution in 2005–2009 were scrutinized. Clinicopathological features of patients aged ≤40 years (young patients) at the time of the initial diagnosis were compared to those patients aged >40 years (older patients), and there was double the number of older than younger patients. In a period of 5 years, there were 82 (24.6%) young patients (≤40years) out of 33 OSCC patients diagnosed, and the majority being males. The bulk of OSCC patients were found to have chewing habits of tobacco and areca nut products, and the proportion of patients using commercially available pan-tobacco products among young patients were higher when compared to older patients. Exophytic growth was one among the common morphological presentation in OSCC patients, but young patients produced a significantly higher endophytic presentation compared to older patients. There was no significant difference between study patients when histopathological grading systems of Broder and anneroth et al were applied. Exposure due to behavioral risk factors was similar in young and older patients; although these had less time to act in young patients, the lesions were similar in terms of pathology and size. Demographic and clinical parameters like gender, risky habits, duration of risky habits, and tumor morphology were significant predictors in the study subjects. Future studies should regulate the prognostic values of these parameters.

Sadasivan A *et al* [27] [2012] verrucous lesions of the oral cavity can be of different histopathology. The present study evaluates the clinico-pathological features of verrucous lesions of the oral cavity and analyses the treatment outcomes. This is a retrospective study of 15 consecutive patients who were diagnosed with verrucous lesions of the oral cavity, during the 5-year study period from January 2006 to December 2010. Demographic, clinico-pathological features, treatment plans, and outcomes were analysed. 15 patients with verrucous lesions of the oral cavity were managed with surgery as the primary modality. The mean age

was found to be 62.8 years (range 35-85 years). Wide local excision of the primary lesion with adequate mucosal and soft-tissue margins was carried out with focus on R0 resection to be achieved. Free-flap reconstruction was performed in eight patients. all patients were loco-regionally controlled with good functional speech and swallowing outcome. Verrucous carcinoma of the oral cavity is a distinct clinical entity with varied histopathology. a surgical excision with wider negative margins and appropriate reconstruction is necessary to optimize the disease and functional outcome.

Pires FR *et al* [28][2013] showed that epidemiological data from oral squamous cell carcinoma (OSCC) is mostly from North american, European and East asian populations. The aim of this study was to evaluate the demographic and clinicopathological features from OSCC diagnosed in an Oral Pathology Department in southeastern Brazil in an 8-year period. all OSCC diagnosed from 2005 to 2012 were referred, including histological analysis of all hematoxylin and eosin-stained histopathology slides and review of all demographic and clinicopathological information from the laboratory records. a total of 346 OSCC was retrieved and males dominance of 67% of the sample. Mean age of the patients was 62.3 years-old and females were diagnosed at a decade older than males ($p<0.001$). Mean time of complaint with the Tumors was 10 months and site distribution were found to be in most cases were having primary at that the lateral border of the tongue (37%), alveolar mucosa/gingiva (20%) and floor of mouth/ventral tongue (19%) were the commonest affected sites. Mean size of the Tumors was 3.4 cm, with no differences between males and females ($p=0.091$) and males reported both tobacco and alcohol consumption more commonly than females. Histological grade of the Tumors suggested that 27%, 40% and 21% of the Tumors were, respectively, categorised as well-, moderately- and poorly-differentiated OSCC, 26 cases (7.5%) were microinvasive OSCC and 17 cases were OSCC variants. OSCC in males mostly affected the lateral border of tongue, floor of mouth/ventral tongue and alveolar mucosa/gingival, while they were more common on the lateral border of tongue, alveolar mucosa/gingival and buccal mucosa/buccal sulcus in females ($p=0.004$). The present data reflect the epidemiological characteristics of OSCC diagnosed in a public Oral Pathology department in southeastern Brazil and have highlighted several vital differences in clinicopathological features when comparing both genders of OSCC-affected patients.

Jadhav KB *et al* [29][2013] found that in spite of the vast number of research and the advances, oral squamous cell carcinoma implies highly significant mortality and morbidity rates. This

has motivated the search of factors with prognostic significance. a web based search was initiated for all published and cited articles by using Medline/PubMed, Google Scholar with key words like prognosis, survival rate, risk factors associated with oral squamous cell carcinoma, prognosis of oral squamous cell carcinoma. The search was limited to articles published in English language with no limitation to date of publication. This review was focused on clinical, pathological and molecular factors in association with survival and prognosis of oral squamous cell carcinoma patients. Most articles had described atleast 2 parameters related to prognosis. Taking into consideration the biological behavior and nature of carcinoma, all the parameters were correlated and so could not predict the prognosis independently. Consideration of all the parameters was required to evaluate the prognosis. They hypothesize the combination usage of clinical and pathological indicators together to assess the prognosis. The care givers can evaluate the prognosis in a better and more definitive way by using prognosis assessment sheet.

Montero PH *et al* [30][2015] found that carcinoma of the oral cavity is one of the commonest malignancies worldwide. although early diagnosis is relatively easy, presentation with advanced disease is common and later challenges the treatment due to the extend of the disease infiltration. The treatment of choice is primary surgical resection [wide local resection] with or without plastic surgical reconstruction with or without postoperative adjuvant therapy. Improvements in surgical techniques combined with the routine use of postoperative radiation or chemoradiation therapy have resulted in improved surgical success and survival. Successful treatment is advised on multidisciplinary treatment strategies to maximize oncologic control and minimize effect of therapy on form and function. Prevention of oral carcinoma requires better education about lifestyle-associated risk factors, and improved awareness and techniques for early diagnosis.

Singh MP *et al* [31][2016] detected that oral squamous cell carcinoma (OSCC) ranks 12th commonest carcinoma in the world. The aim of this evaluate was to retrospectively assess the OSCC. a retrospective study of 611 OSCC patients from January 2010 to December 2013 was conducted out in Department of Surgical Oncology, King George's Medical University, Lucknow, India. Details of patient's sex, age, tobacco habit and site of carcinoma were assessed. Data were analysed by Student's t test and chi-squire [$\chi 2$] test. The prevalence of OSCC was significantly ($p < 0.001$) higher in males [75.9%] than females [24.1%]. The mean age of female patients was more than males ($p < 0.001$). In both the genders, the buccal mucosa and gingivobuccal sulcus were found to be the most affected sites. Moreover, the smokeless

form of tobacco was found to be significant association with OSCC, especially in females. The study summarised that OSCC is more common in men when compared to women, probably due to habit of tobacco consumption. Chewing tobacco use is an important risk factor, especially in females.

Ampur OY *et al* [32][2016] observed that oral cavity carcinoma is considered as a major health problem worldwide and has been associated with high local recurrence rate and poor prognosis. Oral cavity squamous cell carcinoma (OCSCC) in Sanglah General Hospital Denpasar contributed to 71.7% of all head and neck carcinoma from 2002-2011 with an increasing trend yearly. advances in their understanding of OCSCC have not significantly improved the outcome in OCSCC management. Therefore, many studies have aimed on the roles of biomolecular markers in OCSCC. One of biomolecular marker that has been the focus of many OCSCC researches is p16. This was an analytic cross-sectional study with 50 subjects to determine the association of p16 expression with age group, Tumor site, stage, and grade in OCSCC. Data was analysed descriptively and the association between variables were analysed with Chi-Square or Fisher's Exact Test with a p value. Out of the total 50 patients OSCC, age ranged from 33 to 89 years with mean age of 64.24 years and more than half of the subjects were males [52%]. Lower lip was the commonest site of the Tumor and then came upper lip and tongue at 42%,26%,18% respectively. Most of it being moderately differentiated at 54%. Upon analysis, 84% of the patients showed negative expression of P16 but Ki67 expression was positive among 76% of the subjects.

Peng Q *et al* [33][2016] observed that oral verrucous carcinoma (OVC) is a verrucous variant of OSCC, which tallies for 2-12% of all oral carcinomas with a 5-year survival rate of only nearly 50%. Enormous effort has been dedicated to this carcinoma, and the past few decades have witnessed major improvisation in relevant diagnostic and therapeutic demands. Currently, there exist three main challenges from primary sub-fields of research and clinical practice of the carcinoma, as multifactorial etiology, complex molecular mechanism, and inadequacy in treatment. This study reviews the already existing literature on the oral carcinoma, encompassing its etiology, clinical presentations and pathology, molecular mechanism, diagnosis and differential diagnosis, and management. For improved treatment of OVC, multifactorial etiology analysis, incorporation of effective biomarkers for mechanism illustration, and combination of multidisciplinary modalities are expounded, in an attempt to minimize the challenges and to favour a useful guide for future research in the field of oral carcinoma.

Jin X *et al*[34][2016] found that this study was to analyse clinicopathological risk factors associated with the grave outcome of OSCC in a large cohort of Chinese patients, and to construct tissue microarrays (TMAs) with the help this cohort. Univariate and multiple logistic regression analyses were conducted to evaluate the predictors of poor prognosis in a cohort of 232 patients with OSCC, following which the patient tumor tissues were used to construct TMAs. Univariate logistic regression analysis indicated that a poor outcome of OSCC had significant association with the male gender, a history of smoking, the tumor-node-metastasis stage and cervical lymph node metastasis. Multiple logistic regression analysis showed that a greater risk of mortality in patients with OSCC was significantly and independently associated with cervical lymph node metastasis (odds ratio, 3.421; 95% confidence interval, 1.609-7.27). Thus, the results of the current study suggested that cervical lymph node metastasis is an independent risk factor associated with a poor prognosis of OSCC patients. TMAs of OSCC were successfully developed, and are the first TMAs to be published upon mainland Chinese patients.

Feng Z *et al* [35][2017] found that the aim of this study was to explore the clinicopathological features, risk factors, and treatment of poorly differentiated OOSCC patients in the northern Chinese population. a sum of 118 poorly differentiated OOSCC patients from 2236 consecutive cases were retrospectively assigned for this study. Cox regression analysis showed that location [hazard ratio [HR]: 2.561, 95% confidence interval [CI]: 1.064-6.164, p = 0.036] and cervical lymph node ratio (LNR) (HR: 3.915, 95% CI: 1.797-8.530, p = 0.001) were independent predictive aspects for 5-year disease-specific survival (DSS). LNR >0.036, oropharynx site, and advanced clinical stage express a model of risk stratification. The patients with a risk score of ≥2 were noted as the high-risk population, and patients with a risk score of 0 or 1 were identified as the low-risk population. Patients in the high-risk population who had undergone surgery plus concurrent chemoradiotherapy (CCRT) had markedly better 5-year DSS than those who only underwent surgery (60.0% vs. 20.0%, p = 0.016). However, subjects in the low-risk population who underwent surgery alone showed a similar 5-year DSS (68.2%) compared with those who received both surgery and radiotherapy (RT) (68.2%) or surgery and CCRT [50.0%] (p = 0.907). High LNR, oropharynx site and advanced clinical staging formulates a model of risk stratification for patients with poorly differentiated OOSCC. If two or more risk factors are present, surgery and adjuvant chemoradiotherapy can give the better prognosis.

Majumdar B *et al* [36][2017] found that even after diagnostic and therapeutic advancements, disease and death rates in the patients diagnosed with oral carcinoma remain static. Hence, an

understanding of the factors that predict the progression of oral carcinoma appears to be useful in determining on the most appropriate therapy, thereby improving survival. To do so in practice, a critical knowledge of prognostic markers that have high sensitivity is indispensable. Though recent advancement in research has introduced newer molecular markers, challenging the conventional prognostic assessment techniques their universal application is yet to be concluded. In practice, clinical and histopathological parameters are generally used for choosing treatment strategies and for concluding the prognosis in oral carcinoma patients. literature research yielded a multitude of parameters that can be involved in the determination of prognosis of a patient. Based on published evidence, factors of higher significance were pTNM, tumor volume, depth of invasion, surgical margin status whether being negative or positive, tumor budding, vascular and perineural invasion, medullary bone invasion, extracapsular invasion, and the presence of distant metastasis.

Padma R *et al* [37][2017] observed that in developing countries, oral squamous cell carcinoma is a leading cause of mortality due to late presentation and diagnosis. Hence, the aim of the study was to analyse the clinical and pathological presentation of buccal mucosa carcinoma patients. a case series study was held in regional carcinoma centre, Tamil Nadu. Demographic and clinical details were summed up from medical registries between 2013 and 2015. The present study consists of 198 cases which have 125 [63.1%] male and 73 [36.9%] female. The mean age of the cases was 54.16 ± 17.25 years. Histopathology reports showed most frequency of well-differentiated buccal mucosa squamous cell carcinoma 98 [49.5%] and followed by moderately differentiated 98 [34.3%] and poorly differentiated 32 [16.2%]. Clinical tumor nodal metastasis reports suggested 168 [85%] of advanced clinical stage (III and IV) of buccal mucosa carcinoma, whereas only 30 [15%] was presented at early stage (I and II) of disease. Based on the clinicopathological analysis, 86 [43.4%] patients were fit for surgery and followed by adjuvant chemo-radiotherapy. Of 198 cases, the commonest clinical complaints were identified with 73 [38%] pain and followed by 47 [28%] bleeding, may be due to unawareness or negligence towards the disease. The study summarized that most of the cases were diagnosed in advanced stage of tumor with severe pain and bleeding. Hence, further studies warrant the need for awareness of clinical symptoms and also to analyse the risk factors for delay in diagnosis in Tamil Nadu population, which might reduce morbidity and mortality.

Farrag a *et al* [38][2018] observed that this study shows the epidemiological data and clinico-pathological features of oral carcinoma in patients treated in Prince Sultan Military Medical City- Oncology Department over the last 7 years. They reviewed all available data in their

electronic and paper files for patients who had a confirmed histopathological diagnosis of oral cavity malignancies between 2009-2015. a total of 87 patients with histopathologically confirmed oral carcinoma. The majority of patients were males (M:F = 1.63:1). Median age at time diagnosis was 62 years (24-95). History related to risk factors was finished in only 59 patients [68%]. Forty-five patients [76%] had an associated history for tobacco consumption either smoking and/or chewing (shamma). The use of shamma, [a mixture of powdered tobacco, lime, ash, black pepper, oils and flavorings], was isolated in 31/59 patients [either alone or combined with smoking]. Oral Tongue as a primary site represents approximately half of the patients 44 [50.6%], followed by alveolar ridge [16.1%] and floor of mouth [11.5%], buccal mucosa [10.3%] and other sites [11.5%]. Two thirds of patients [66.6%] presented with advanced stages [III and IV]. The 5-year overall survival rate was 77.1% for the early stage disease group and 45.9% for the advanced stage disease group [P = 0.028]. The 5-year disease-free survival rate was 65.6% for the early stage disease group compared with 28.1% for the advanced stage disease group [P = 0.02]. Most of their cases had a positive association ~~history~~ of tobacco usage. This together with the higher percentage of advanced diseases that carried a significantly poor outcome warrant the need for much more effective anti-tobacco campaigns, public awareness and primary care physicians education for early detection of disease.

Nóbrega TD *et al* [39][2018] showed that early detection of oral carcinoma is the most effective means of reducing morbidity, complexity, and extent of treatment and prognosis. This study assessed the clinicopathological profile of epidermoid carcinoma of the tongue, including treatment and survival. This observational, retrospective cross-sectional study assessed patients with squamous cell carcinoma of the tongue treated at the Dr. Luiz Antônio Hospital, Natal, Brazil, from January 2001 to December 2011. Survival variables were calculated with the help of Kaplan-Meier method and compared by log rank tests. Of the 412 patients diagnosed in this period, 298 [72.3%] were men; their mean age was 60.5 years, and 69.2% were diagnosed with advanced stage III/IV tumors. Improved survival was associated with early stage diagnosis, absence of lymph nodes metastasis at diagnosis, and treatment with surgery alone. Late stage diagnosis of oral carcinoma inversely affects patient survival. In addition, the general public should be made aware of the factors for prognosis for oral SCC of the tongue and of the importance of periodic examinations of the oral cavity

Liu T *et al* [40][2019] observed that the volume-outcome relationship is a well-known phenomenon in surgical oncology. The purpose of this study was to quantify the impact of surgeon volume on the management outcome of oral squamous cell carcinoma [OSCC]

patients. all new OSCC cases managed with curative intent between 2008 and 2013 were taken for study. a heterogeneous set of predictor variables was assessed, including patient, tumor and treatment factors. The results of interest were recurrence-free survival [RFS], overall survival [OS] and disease-specific survival [DSS]. To investigate the cut-off in surgeon volume, the number of OSCC resections was evaluated in multiplies of 5 cases per annum as per DSS, using univariable regression analysis. 534 cases were allotted. Independently, the significant negative predictors for patient survival were age, perineural invasion, worsening tumor staging, and extracapsular spread. High-volume surgeon was determined to be most significant at 20 cases per annum and have significant association with improved RFS [HR: 0.67], OS [HR: 0.44], and DSS [HR: 0.39]. Results from this study support the rationalisation of OSCC treatment at high-volume centres and in the hands of experienced surgeons for better patient survival. Head and neck surgeons should be performing not less than 20 OSCC cases per year to maintain competency in OSCC ablation.

Durrani S *et al* [41][2020] showed that oral carcinoma is the 3rd commonest cause of malignancy in Saudi arabia after lymphoma and leukemia. The high incidence rate of oral carcinoma in this region is attributed to frequent use of chewable and smokable tobacco [Shamma]. In this report they have reviewed the management and subsequent outcome of 228 oral carcinoma patients at the Oral Maxillofacial Surgery department of the armed Forces Hospital, Riyadh, Kingdom of Saudi arabia. In this retrospective study the case notes of 228 oral carcinoma patients managed at the armed Forces Hospital, Riyadh were reviewed. age, sex, presenting complaints, site of carcinoma in oral cavity, habit of tobacco chewing, mode of treatment and complications as a result of treatment were recorded. Out of 228 patients 149 were males and 79 were females with age varying from 23 to 82 years. The majority of patients [58%] had associated tobacco chewing habit. Most of the patients received radiation therapy [98%] and at times with adjuvant chemotherapy. 73% of patients underwent surgery followed by radiotherapy, whereas 2% had surgery alone. Recurrence of the disease was found in 56% of the patients over a time period of 5 years following primary treatment. a close association between tobacco chewing and oral carcinoma was elicited. It is concluded that post operative radiotherapy is a highly successful method of treatment in patients with oral carcinoma. Cases with a history of shamma [chewable tobacco] usage did not show signs deep invasion even when the Tumor was large. They also showed good prognosis after wide local excision but more resistant to radiotherapy comparing with those cases with no history of shamma usage.

Borse V *et al* [42][2020] found that globally, oral carcinoma is the sixth commonest type of carcinoma with India contributing to almost one-third of the total cases and the second country having the largest number of oral carcinoma cases. Oral squamous cell carcinoma [OSCC] dominates all the oral carcinoma cases with potentially malignant disorders, which is also recognized as a significant pre-clinical phase of oral carcinoma. Tobacco consumption as smokeless tobacco, betel-quid chewing, excessive consumption of alcohol, inadequate oral hygiene and prolonged viral infections that include the human papillomavirus [HPV] are some of the risk factors for the occurrence of oral carcinoma. Lack of knowledge, variance in exposure to the environment, and behavioural risk factors indicate a wide variation in the global incidence and increase the death rate. Various risk factors related to the occurrence of oral carcinoma, the statistics of the distribution of oral carcinoma in India by various virtues, and the socio-economic positions. Multiple conventional diagnostic techniques used routinely for detection of the oral carcinoma are discussed along with advanced techniques.

Anwar N *et al* [43][2020] oral squamous cell carcinoma [OSCC] has the highest prevalence in head and neck carcinomas and is the first and second commonest carcinoma in males and females of Pakistan respectively. Major risk factors include tobacco chewing habits like areca nut, betel quid, and tobacco. The large number of OSCC presents at an advanced stage with poor prognosis. On the face of such a large burden of this preventable carcinoma, there is a relative deficiency of recent robust data and its association with known risk factors from Pakistan. The aim of this study was to observe the socioeconomic factors and clinicopathological features that may lead to the development of OSCC. a total of 186 patients diagnosed and treated at a tertiary care hospital, Karachi Pakistan were assessed. Clinicopathological and socioeconomic information was obtained on a structured printed questionnaire. Descriptive investigation was done for demographics and socioeconomic status [SES] while regression analysis was performed to analyse the association between SES and chewing habits, tumor site, and tumor stage. Most of patients were males and the mean age of OSCC patients was 47.62±12.18 years. Most of the patients belong to low SES [68.3%] and 77.4% were habitual of chewing tobacco. Gender [male] and SES were significantly associated with chewing tobacco habits [$p<0.05$]. Odds of developing buccal mucosa tumors in chewers [of any type of tobacco substance] and gutka users were 2 and 4 times higher than non-chewers respectively. Middle age, chewing tobacco habits, and occupation had significant association with late stage presentation of OSCC [$p<0.05$]. In conclusion, male patients belonging to low SES in their 40-year age who had chewing tobacco habits for years constituted the majority of

OSCC. Buccal mucosa was the commonest site in chewers and the majority presented with late stage tumors.

Siriwardena BS *et al* [44][2020] Lymph nodal metastasis is a critical prognostic factor in predicting the prognosis of oral squamous cell carcinoma [OSCC]. When patients present with a clinically positive neck, the treatment of choice is modified radical neck dissection. However, management of a clinically negative neck is still a topic of significant controversy. This study was conducted in order to propose a model for predicting regional lymph node metastasis of OSCC using histological parameters such as tumor stage, tumor size, pattern of invasion [POI], differentiation of tumor, and host immune response, along with the expression levels of six biomarkers [periostin, HIF-1α, MMP-9, β-catenin, VEGF-C, and EGFR], and, furthermore, to compare the effect of all these parameters on recurrence and 3 yr and 5 yr survival rates. Histological materials obtained from the archives were used to analyse histological parameters and immunohistochemical profiles. conventional methods were used for immunohistochemistry and for analysing the results. Data related to recurrence and survival [3 and 5 years] was also collected. Clinical data was obtained from patients' records. Male to female ratio was found to be 3 : 1. The most common site of OSCC was the buccal mucosa, and majority of them were T3 or T4 tumors presented at stage 4. 62.5% of the tumors were well differentiated. Three-year and 5-year survival rates were significantly associated with cervical lymph node metastasis and recurrence. POI was significantly related with tumor size, stage, 3-year survival, EGFR, HIF-1α, periostin, and MMP-9. Expression of EGFR detects a direct association with metastasis. POI, level of differentiation, and expression of EGFR are independent prognostic markers for cervical lymph node metastasis. Therefore, these parameters may help in management planning of a clinically negative neck.

Tseng YJ *et al* [45][2020] found that a tool for precisely categorizing postoperative patients with advanced oral carcinoma is important for the treatment plan, such as intensifying or deintensifying the regimen to improve their quality of life and outcome. To develop and validate a machine learning–based algorithm that can facilitate survival risk stratification for patients with advanced oral carcinoma who have comprehensive clinicopathologic and genetic data. In total, comprehensive clinicopathologic and genetic data [consisting of clinical, pathologic, and 44 carcinoma-related gene variant profiles] of 334 patients with stage III or IV oral squamous cell carcinoma were considered to develop and validate the algorithm in this 15-year cohort study. Data analysis was done between February 1, 2018, and May 6, 2020. The main results were carcinoma-specific survival, distant metastasis–free survival, and

locoregional recurrence–free survival. Model performance was compared in terms of the information criterion and the Harrell concordance index [C index]. Complete data were present for 334 patients [315 men; median age at onset, 48 years [interquartile range, 42-56 years]]. The predictive models using comprehensive clinicopathologic and genetic data outscored those using clinicopathologic data alone. In the groups of postoperative patients receiving adjuvant CCRT, the models demonstrated higher classification score than those using clinicopathologic data alone in carcinoma-specific survival [mean [SD] C index, 0.689 [0.050] vs 0.673 [0.051]; P = .02] and regional recurrence–free survival [mean [SD] C index, 0.693 [0.039] vs 0.678 [0.035]; P = .004]. The classification performance in distant metastasis–free survival was same [mean [SD] C index, 0.702 [0.056] vs 0.688 [0.048]; P = .09]. a risk stratification model using comprehensive clinicopathologic and genetic data precisely differentiated the high-risk group from the low-risk group in carcinoma-specific survival and locoregional recurrence–free survival for postoperative patients with advanced oral carcinoma. This algorithm can be used through an online calculator to provide additional custom information for postoperative management of patients with advanced oral squamous cell carcinoma.

Okuyama K *et al*[46][2021] evaluated that this study is to report the differences in clinicopathological features of oral tongue squamous cell carcinoma [OTSCC] and survival among adolescent and young adult [AYA] patients and elderly patients and to find the prognosticators. The medical records of 101 AYA patients and 175 control patients with OTSCC who underwent surgery were considered for study. Variables related to prognosis and their clinicopathological associations were analysed. The 5-year overall survival [5y-OS] rates of AYA and control subjects with stage I and II OTSCC were 94.4% and 89.6% [*P* = .353], respectively, and their 5-year disease-free survival [5y-DFS] rates were showing 82.0% and 76.6%, respectively [*P* = .476]. The 5y-OS rates of patients with advanced stages III and IV OTSCC were 83.3% and 66.7% [*P* = .333], respectively, and their 5y-DFS rates were 75.0% and 57.1% [*P* = .335], respectively. Logistic regression analysis showed that there was no significant clinicopathological difference in AYA and control group. Furthermore, there was no significant difference in 5y-OS rates between patients who had undergone elective neck dissection [END] and those who had undergone therapeutic neck dissection [TND] in both group [*P* = 0.717 and 0.688]. Overall, the present study suggested the clinicopathological features and prognosis of OTSCC were similar in AYA patients and elderly patients. Moreover, as there was no significant difference in OS between patients who had undergone END and

those who underwent TND in AYA and control groups, their results suggest that the indication for END in AYA patients with clinical N0 OTSCC is as same as that for elderly patients.

Yang SW *et al* [47][2021] observed that the tongue is corresponds a high-risk site for oral leukoplakia and malignant transformation. The aim of this study is to evaluate the clinicopathological characteristics and management outcomes of tongue leukoplakia and evaluate the factors related to recurrence and malignant transformation. 144 patients who received CO2 laser surgery for tongue leukoplakia from 2002 to 2019 were evaluated statistically. The follow-up period was 54.90 ± 54.41 months. Thirty patients resulted in postoperative recurrence [20.83%], and 12 patients advanced into malignant transformation [8.33%]. The yearly transformation rate was 2.28%. Univariate analysis showed that a history of head and neck carcinoma, size of lesion area, clinical presentation, and histopathology were significant factors for both recurrence and malignant transformation. In the multivariate logistic regression, a past history of head and neck carcinoma and size of lesion area were independent prognostic factors for recurrence, and a past history of head and neck carcinoma was the only independent factor for postoperative malignant change. Clinicians should adopt more aggressive strategies for tongue leukoplakia patients with past history of head and neck carcinoma.

Shinohara S *et al*[48][2021] studied to investigate clinicopathological characteristics and survival outcomes of patients with buccal mucosa carcinoma in Japan. This study was conducted with the help of a database of 1055 patients with oral carcinomas treated between 2010 and 2017 at 12 institutions in Japan. 92 patients [8.7%] with primary buccal mucosa carcinoma were extracted and clinicopathological characteristics and survival outcomes were compared among patients with buccal mucosa carcinomas and patients with other oral carcinomas. ages were significantly higher in the patients with buccal mucosa carcinoma [73 years old vs. 69 years old]. Buccal mucosa carcinoma had less advanced cT stage and cN stage than other oral carcinomas. Overall 5-year survival [OS] was 80.6%, and recurrence-free 5-year survival [RFS] of buccal mucosa carcinomas was 67.8%, and there were no significant differences in survival when compared with other oral carcinomas in terms OS or RFS [5y-OS: 82.5%, 5y-RFS: 74.4%]. However, patients with stage IV buccal mucosa carcinoma showed poorer prognosis in terms of OS and RFS compared with the similar stage patients with other oral carcinoma. advanced T stage was the only aspect independently associated with both OS and RFS of patients with buccal carcinoma in this study. Postoperative radiotherapy or chemoradiotherapy should be taken in to consideration to improve survival outcome of buccal

mucosa carcinoma patients, especially for the patients with advanced primary site disease or a higher carcinoma stage.

Chao TY *et al* [49][2021] studied to analyse the clinicopathologic factors affecting the clinical outcomes in histopathological T4aN0 [pT4aN0] buccal mucosal or gingival squamous cell carcinoma [SCC]. This was a retrospective study of 113 consecutive patients who were diagnosed with pT4aN0 buccal mucosal or gingival SCC between January 2010 and November 2018. The median follow-up period was 38 months [range, 1–119 months]. Kaplan-Meier and Cox proportional-hazards models were utilized for survival analysis. In the complete study, 5-year overall survival [OS] and disease-free survival [DFS] rates were 73.7% and 83.6%, respectively. Univariate analysis showed that lymphovascular invasion [LVI], perineural invasion [PNI], and specimen margin status had significant effects on the DFS rate, and Tumor cell differentiation had a significant impact on OS rate. Multivariate Cox regression analysis showed margin status was the only significant factor affecting DFS. The patients [n=38] without the inadequate margin, LVI, PNI, and poorly differentiated tumor cells had a better 5-year DFS rate [P=0.023] whether they had received adjuvant treatment or not [91.5% versus 100%]. However, no significant impact on the OS rate was found [P=0.544]. The patients who had no adverse pathologic factors resulted in fair DFS rate without adjuvant therapy. The adjuvant therapy shall not be considered for this subgroup.

Peña-Cardelles JF *et al* [50][2022] showed that the clinicopathological value of programmed cell death-ligand 1 [PD-L1] expression in the oral squamous cell carcinoma [OSCC] has originated the research of different studies that try to elicit the real relationship between this disease and this immune checkpoint since the latest clinical trials have suggested possible improvisation in the blockade of this immune checkpoint via immunotherapy.

Pallavi K *et al* [51][2022] showed that tongue carcinomas account for 25%–40% of intraoral squamous cell carcinomas [OSCCs]. although TNM staging systems is a global standard for carcinoma reporting, prognosis evaluation, and treatment planning, multiple histopathological risk assessment predictors like tumor thickness (TT), tumor shape, tumor growth pattern, and invasive malignancy grading scoring systems have been evaluated and should form a basis for prediction and prognostication of those aggressive carcinomas. To evaluate and characterize the histomorphological prognostic indicators in OSCCs of tongue and compare it with OSCCs of other anatomic subsites within the oral cavity. Furthermore, to evaluate the significance of histopathological indicators in predicting prognosis of tongue squamous cell carcinomas

(SCCs). 40 SCC cases with 20 in each group of tongue and other intraoral sites were retrieved from department archives. Clinical data and staging were collected for each case. Histomorphological parameters consisting of pattern of invasion (POI), Tumor budding (TB), depth of invasion (DOI), TT, lymphocytic host response, Tumor-associated tissue eosinophilia (TATE), vascular infiltration, perineural infiltration (PNI), and muscular infiltration were assessed. The results were statistically analysed. TB, DOI, and sarcolemmal spread were seen significant histologic predictors in tongue SCC. Upon correlation of histomorphological parameters with clinicopathological staging, TT, POI, and TATE were observed to be significantly correlated ($P \leq 0.05$). The histomorphological risk assessment model may favour an important addition to the existing prognosticators and may be utilized as a prognostic index to help plan and individualize management protocol in cases with aggressive high-risk disease for those whom the use of multimodality treatment seems beneficial.

AIMS

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OBJECTIVES

AIMS & OBJECTIVES

AIM:

To study the clinical-pathological presentation, risk factors, staging, management, and outcome of patients with squamous cell carcinoma of oral cavity

OBJECTIVES:

1. To study the clinical presentation, risk factor and radiological features of the patients with Squamous Cell Carcinoma of Oral Cavity
2. To study the management and outcome of patients diagnosed with Squamous Cell Carcinoma of Oral Cavity.

MATERIALS

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METHODS

MATERIALS AND METHODS

Place of study: Santosh Medical College and Hospitals, Ghaziabad

Sample size: Complete enumeration of cases within study period

Study design: Cross-sectional observational Study

Duration of study: July 2021-June 2022.

Study population: Patients in General Surgery department of SMCH

Inclusion criteria:

- Diagnosed case of Primary Squamous cell carcinoma of Oral cavity of all subsites
- Patients of Both the genders
- Patients of all age groups

Exclusion Criteria:

- Patients who are not willing for the study
- Metastatic Carcinoma
- Carcinoma of Esophagus or any other site in Head & Neck
- HPV related head and neck carcinoma

Methodology:

After taking informed consent from the patient, history of the case including the clinical presentation of their disease with likely etiology and risk factors was taken and followed up with histopathological profile of the patient after doing FNAC/ biopsy and the imaging investigations like CT of face and neck. According to the clinical staging and grade of tumor management was sought and post op the patient was followed up for 30 days period for complications.

Statistical Analysis:

For statistical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS [version 27.0; SPSS Inc., Chicago, IL, USA] and Graph Pad Prism version 5. Data

had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables.

Z-test [Standard Normal Deviate] was used to test the significant difference of proportions.

Once a *t* value is determined, a *p*-value can be found using a table of values from Student's t-distribution. If the calculated *p*-value is below the threshold chosen for statistical significance [usually the 0.10, the 0.05, or 0.01 level], then the null hypothesis is rejected in favor of the alternative hypothesis.

P-value ≤ 0.05 was considered for statistically significant.

RESULT

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ANALYSIS

RESULT & ANALYSIS

Table 9 Distribution of age in group

Age in group	Frequency	Percent
20-29	1	3.1%
30-39	6	18.7%
40-49	11	34.3%
50-59	7	21.8%
60-69	6	18.7%
>70	1	3.1%
Total	32	100.0%

In our study, 1 [3.1%] patient was 20-29 years of age, 6 [18.7%] patient were 30-39 years of age, 11 [34.3%] patient were 40-49 years of age, 7 [21.8%] patient were 50-59 years of age ,6 [18.7%] patients were 60-69years of age and 1 [3.1%] patient was >70 years of age.

The value of z is 3.2026. The value of p is .00138. The result is significant at $p < .05$.

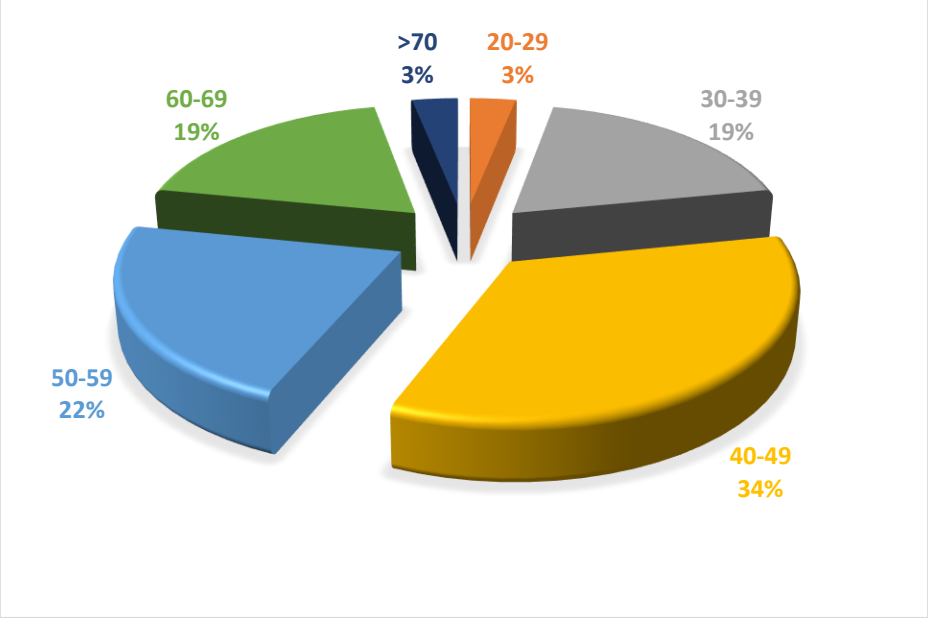

Table 10 Distribution of Sex

Sex	Frequency	Percent
Female	6	18.8%
Male	26	81.3%
Total	32	100.0%

In our study, 6 [18.8%] patients were Female and 26 [81.3%] patients were male.

The value of z is 5. The value of p is < .00001. The result is significant at p < .05.

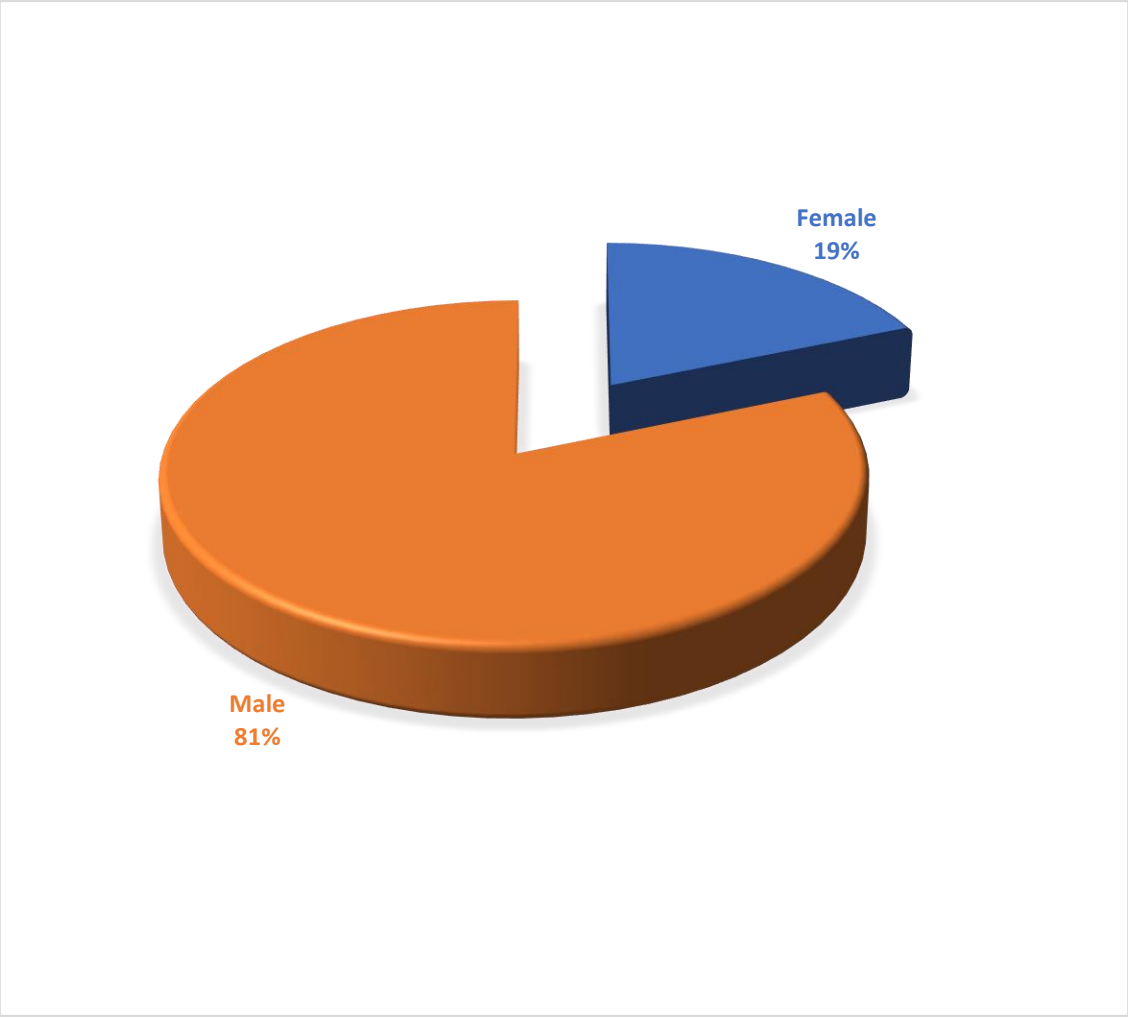

Table 11 Distribution of clinical presentation

Clinical Presentation	Frequency	Percent
Ulcer	32	100%
Swelling	15	46.8%
Trismus	7	21.8%
Bleeding Per Oral	9	28.1%
Sinus	1	3.1%

In our study, 32 [100.0%] patients had Ulcer, 15 [55.0%] patients had Swelling, 7 [21.8%] patients had Trismus and 9 [28.1%] patients had Bleeding Per Oral.

The value of z is 7.7538. The value of p is < .00001. The result is significant at p < .05.

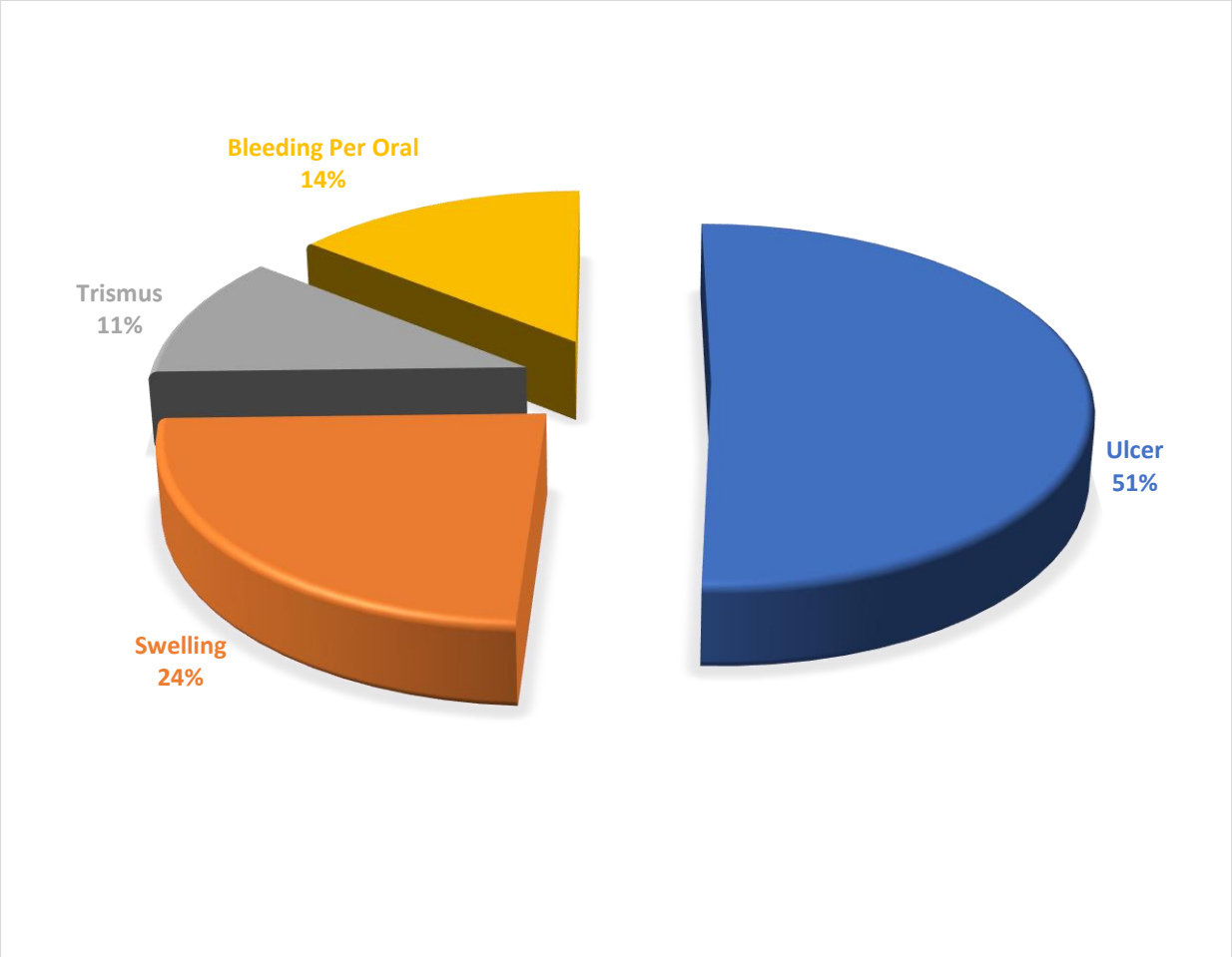

Table 12 Distribution of past history

Past history	Frequency	Percent
Congenital kyphoscoliosis	1	3.1%
Diabetes mellitus	7	21.8%
Hypertensive	2	6.3%
Hypospadias	1	3.1%
Nil	23	71.9%
Total	32	100.0%

In our study, 7 [21.8%] patients had Diabetes mellitus and 2 [6.3%] patients had Hypertensive.

The value of z is 5.6804. The value of p is < .00001. The result is significant at p < .05.

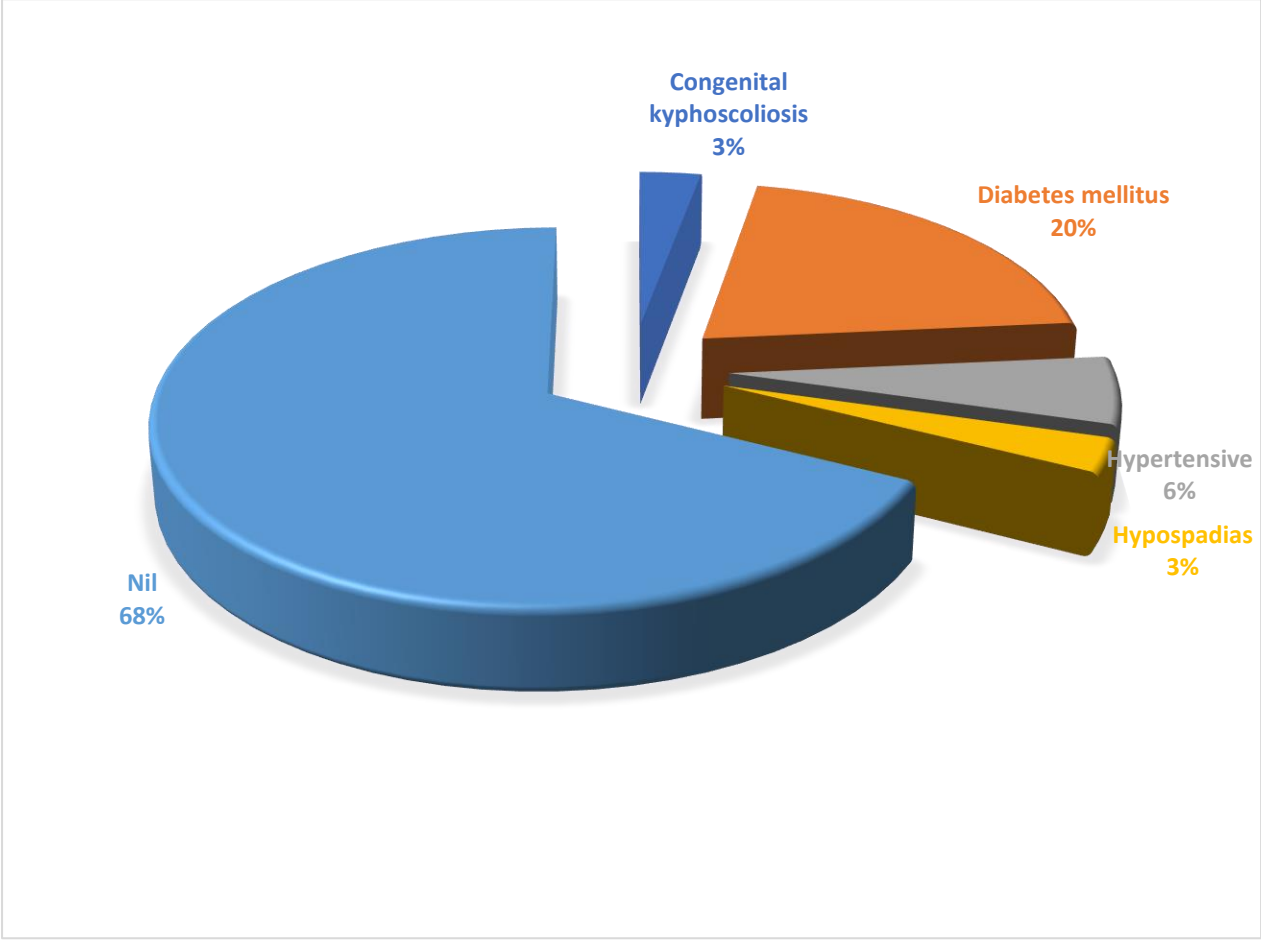

Table 13 Distribution of risk factors

Risk factors	Frequency	Percent
Smoking	23	71.8%
Chewing Tobacco	28	87.5%
Alcohol	11	34.3%
Broken tooth	1	3.1%
Total	32	100.0%

In our study, 23 [71.8%] patients were smokers, 28 [87.5%] patients were Chewing Tobacco and 11 [34.3%] patients were alcoholic.

The value of z is 6.7799. The value of p is < .00001. The result is significant at p < .05.

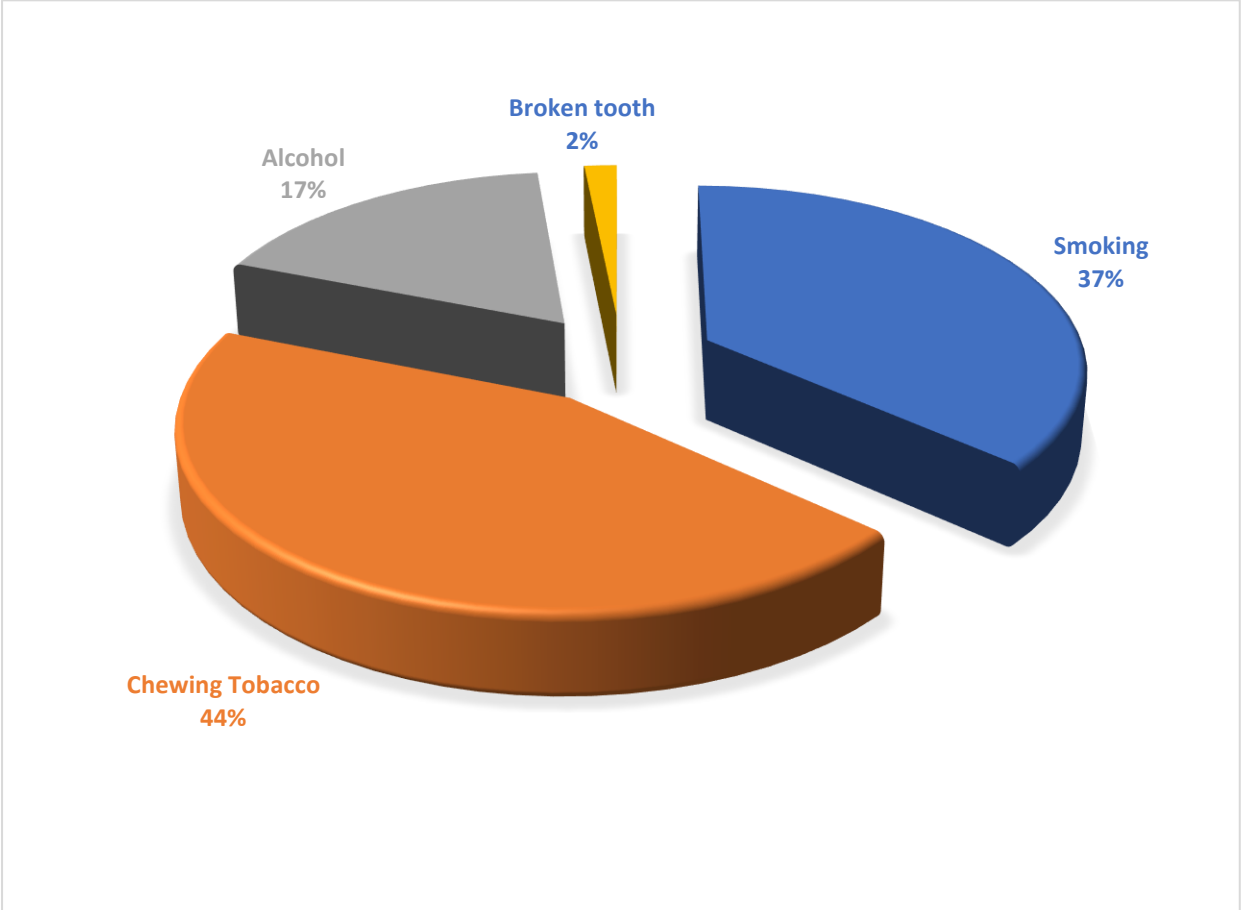

Table 14 Distribution of Premalignant lesion

Premalignant lesion	Frequency	Percent
Erythroplakia	2	6.3%
Leukoplakia	9	28.1%%
Nil	21	65.6%
Total	32	100.0%

In our study, 2 [6.3%] patients had erythroplakia and 9 [28.1%] patients had leukoplakia. The value of z is 4.9498. The value of p is < .00001. The result is significant at p < .05.

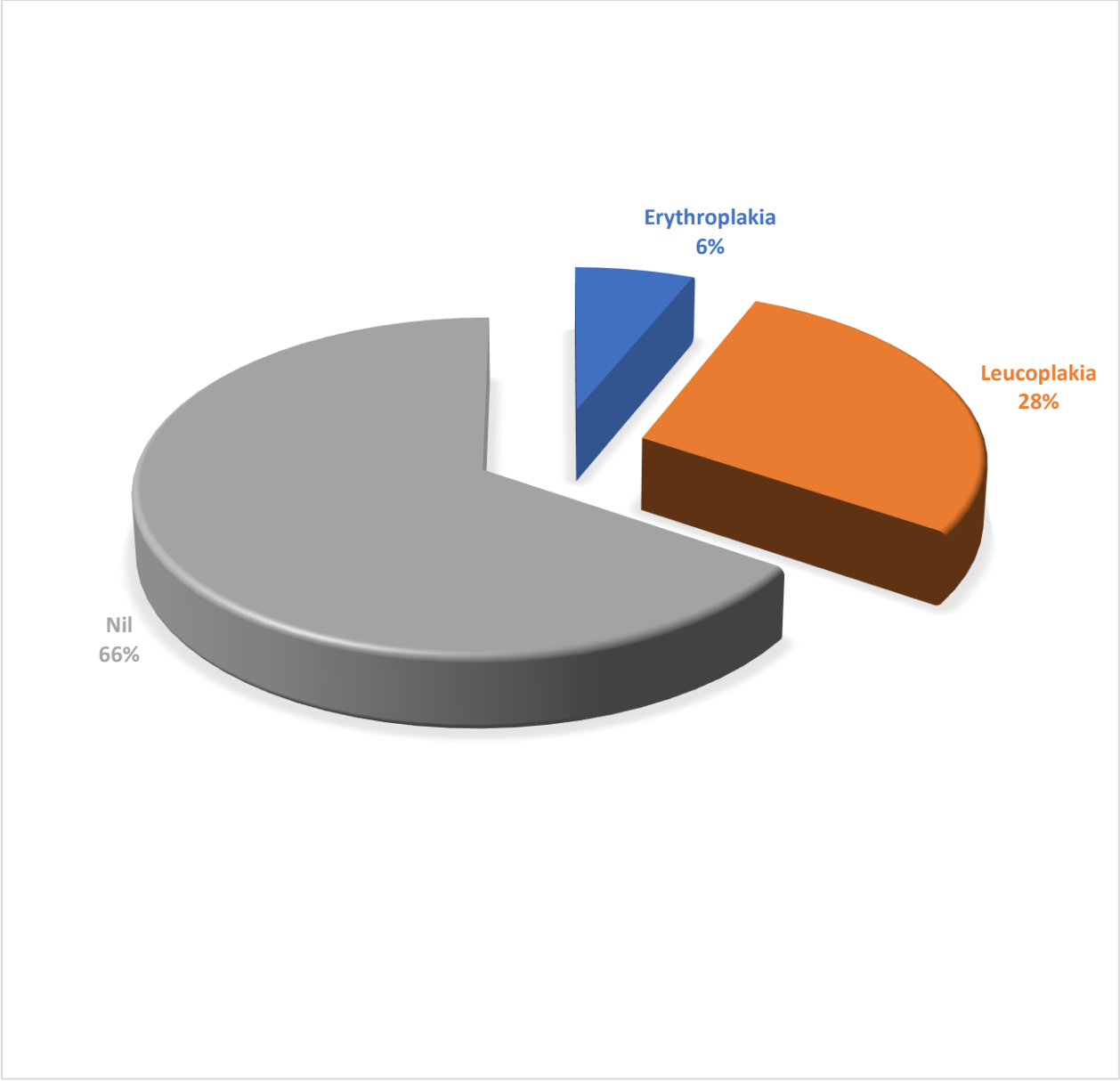

Table 15 Distribution of Subsite

Subsite	Frequency	Percent
Buccal Mucosa	18	56.2%
Tongue	9	28.1%
Retromolar trigone	5	15.6%
Floor of mouth	2	6.2%
Mucosal Lip	2	6.2%
Gingivobuccal sulcus	3	9.3%
Hard palate	2	6.2%
Soft Palate	1	3.1%
Total	32	100.0%

In our study, 18 [56.2%] patients had Buccal Mucosa, 9 [28.1%] patients had Tongue, 5 [15.0%] patients had Retromolar trigone and 3 [9.3%] patients had Gingivobuccal sulcus. The value of z is 4.6511. The value of p is < .00001. The result is significant at p < .05.

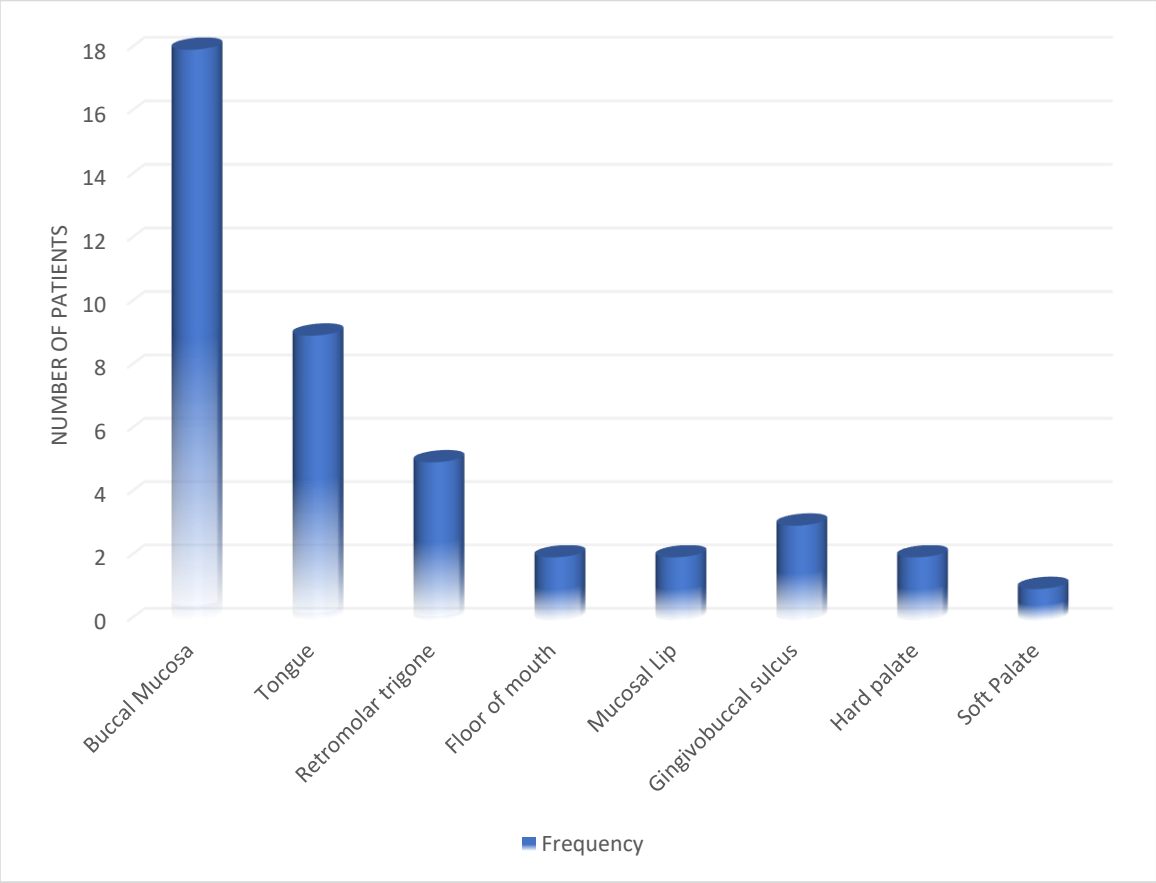

Table 16 Distribution of USG Primary lesion

USG Primary Lesion	Frequency	Percent
No	24	75.0%
Yes	8	25.0%
Total	32	100.0%

In our study, 8 [25.0%] patients had USG Primary Lesion.

The value of z is 4. The value of p is .00006. The result is significant at p < .05.

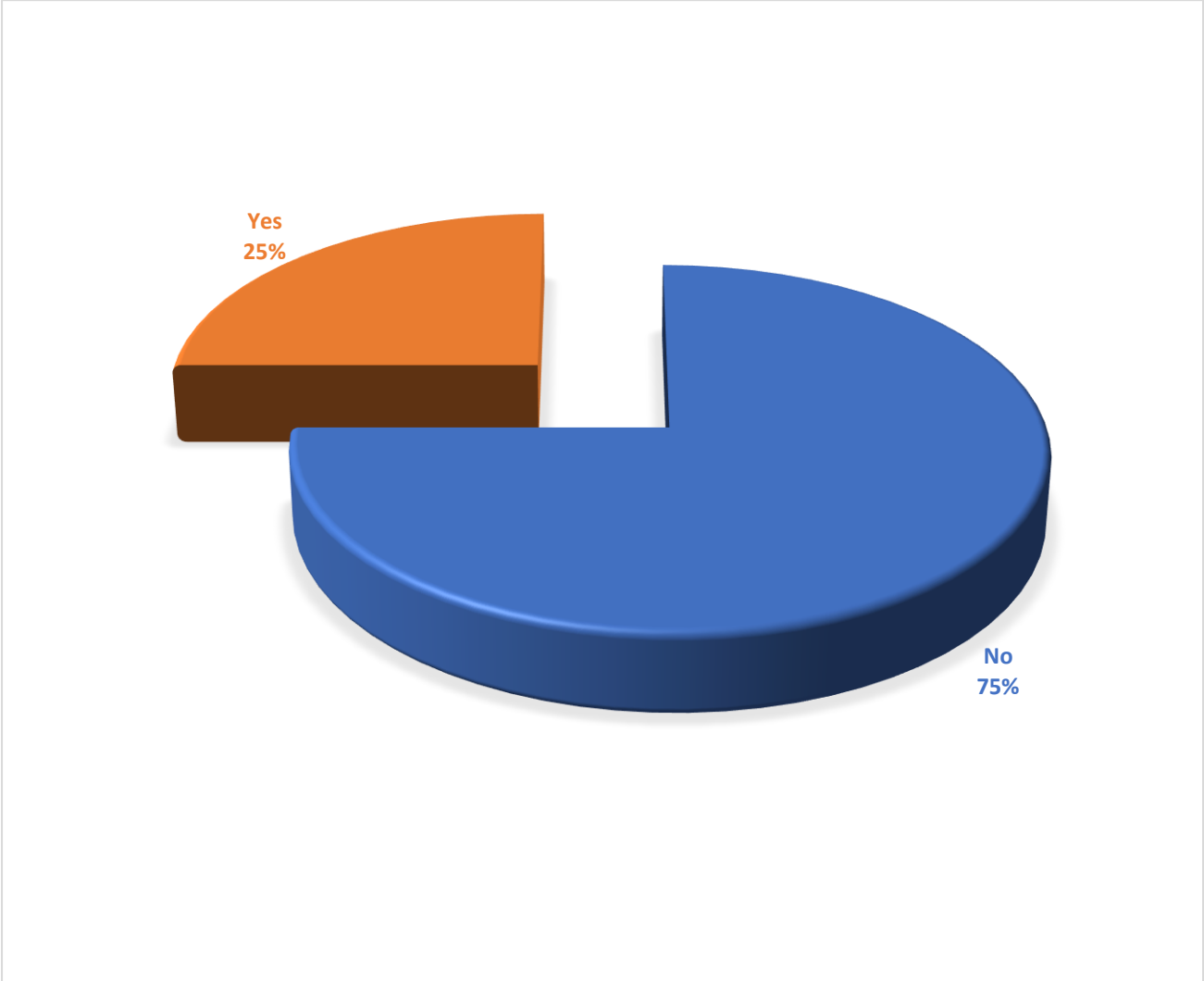

Table 17 Distribution of USG Neck

USG Neck	Frequency	Percent
No	24	75.0%
Yes	8	25.0%
Total	32	100.0%

In our study, 8 [25.0%] patients had USG Neck.

The value of z is 4. The value of p is .00006. The result is significant at p < .05.

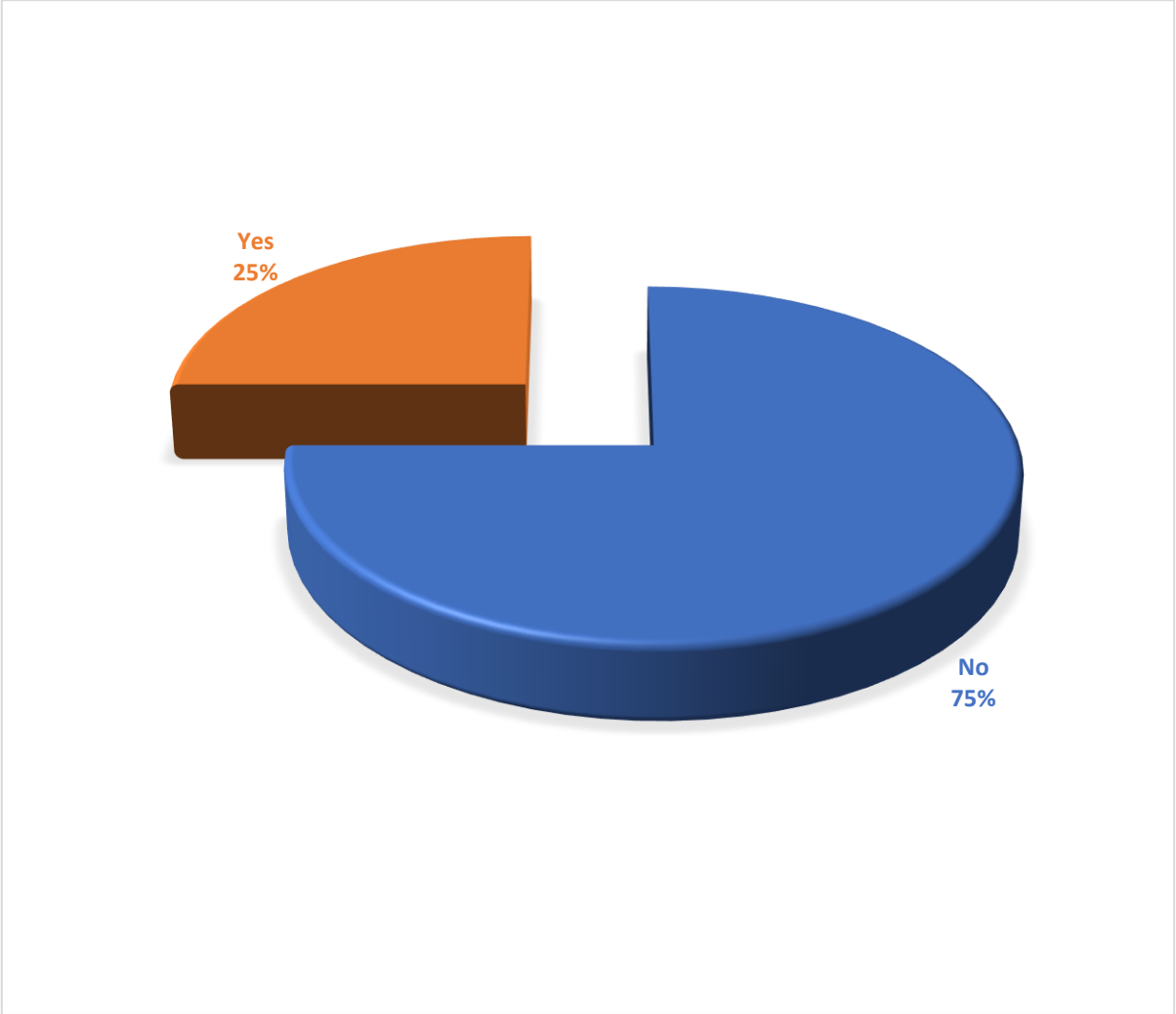

Table 18 Distribution of CT& MRI head and neck

	Frequency	Percent
CT head and neck	23	71.8%
MRI Head and Neck	9	28.2%
Total	32	100.0%

In our study, 32 [71.8%] patients had CT head and neck and 9(28.2%) cases were done with MRI.

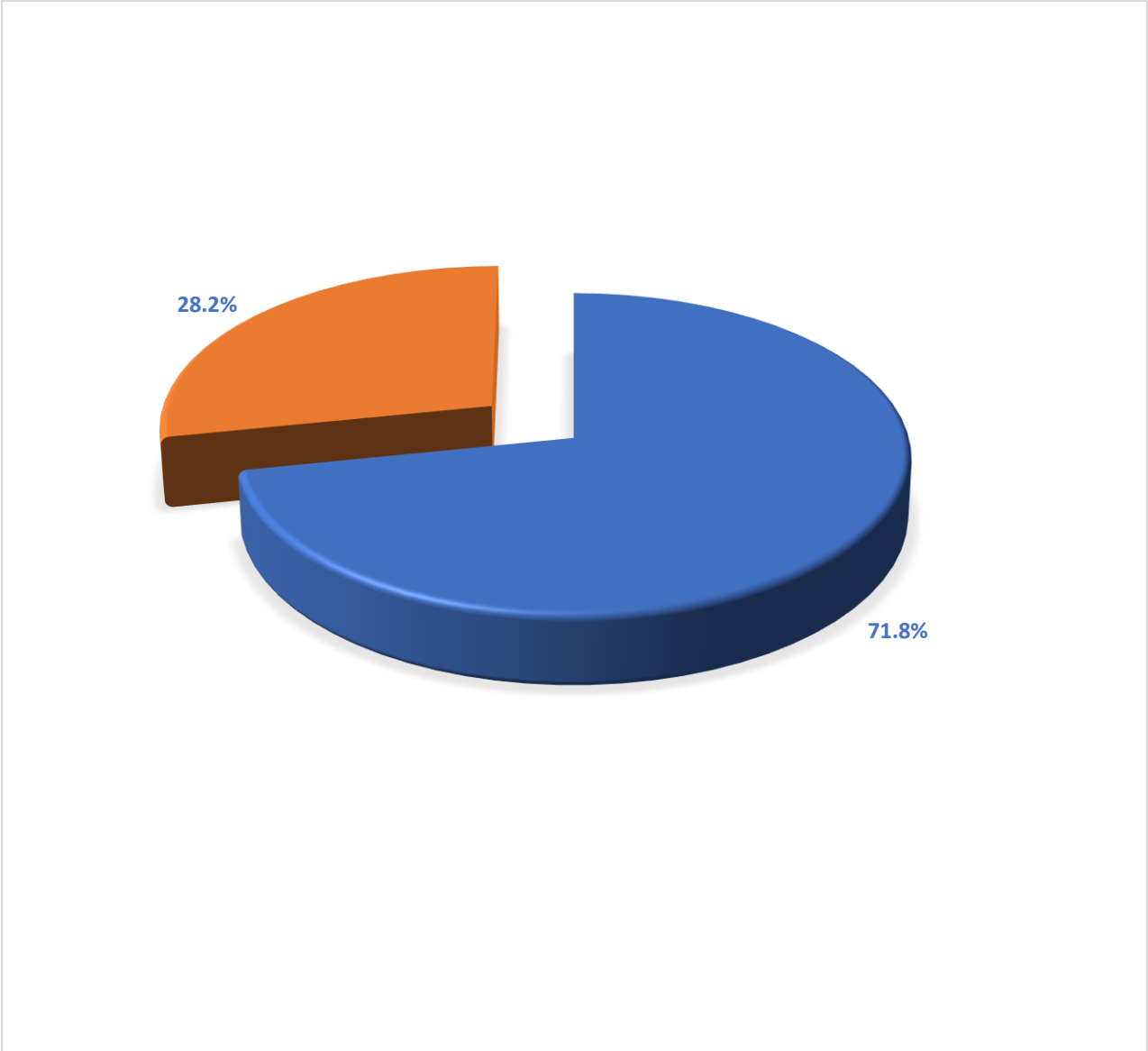

Table 19 Distribution of PET Scan

PET Scan	Frequency	Percent
No	21	65.6%
Yes	11	34.4%
Total	32	100.0%

In our study, 11 [34.4%] patients had PET Scan.

The value of z is 4. The value of p is .00006. The result is significant at p < .05.

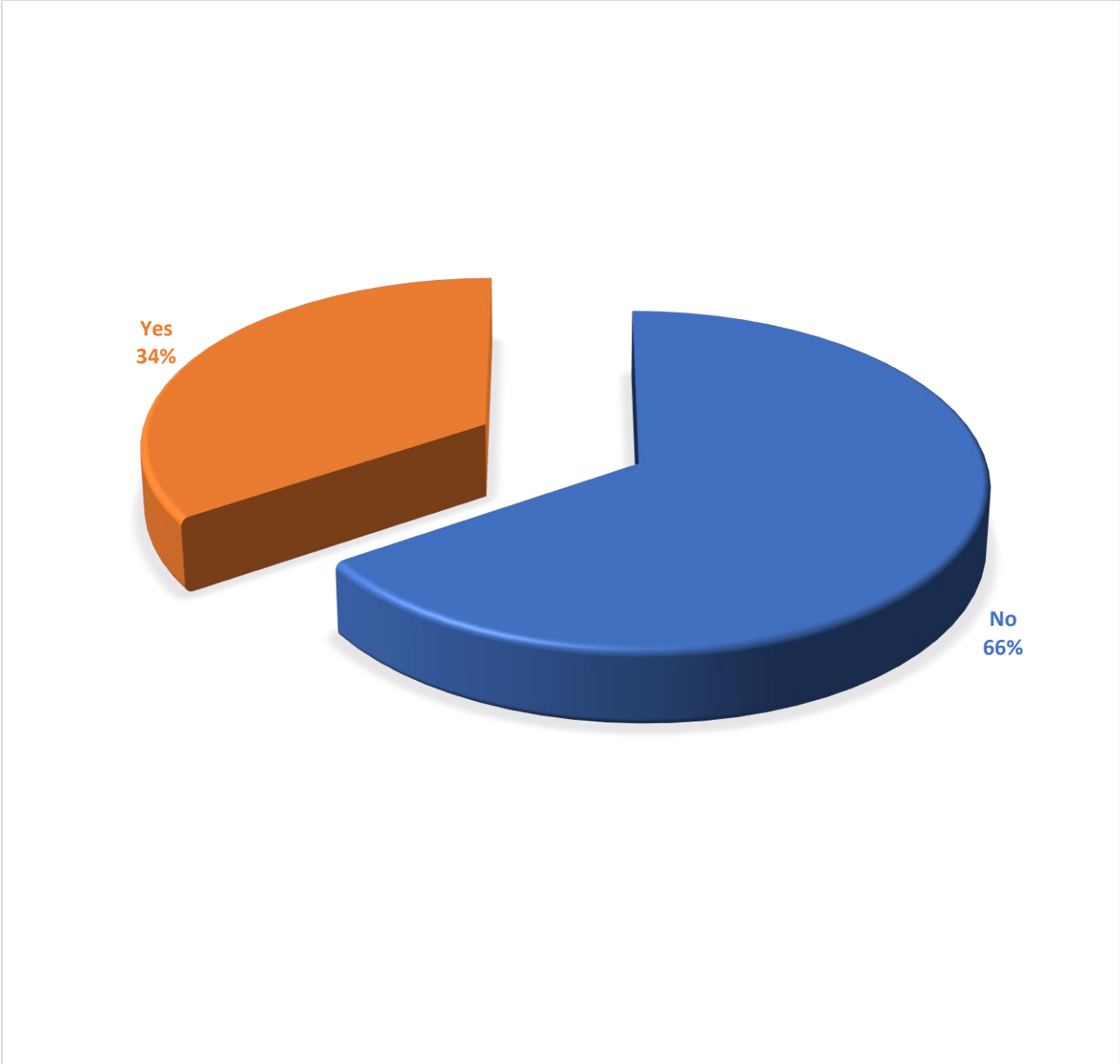

Table 20 Distribution of Nuclear Differentiation

Nuclear Differentiation	Frequency	Percent
Moderately differentiated	2	6.3%
Poorly differentiated	2	6.3%
Well differentiated	28	87.5%
Total	32	100.0%

In our study, 28 [87.5%] patients had Well differentiated.

The value of z is 6.5127. The value of p is < .00001. The result is significant at p < .05.

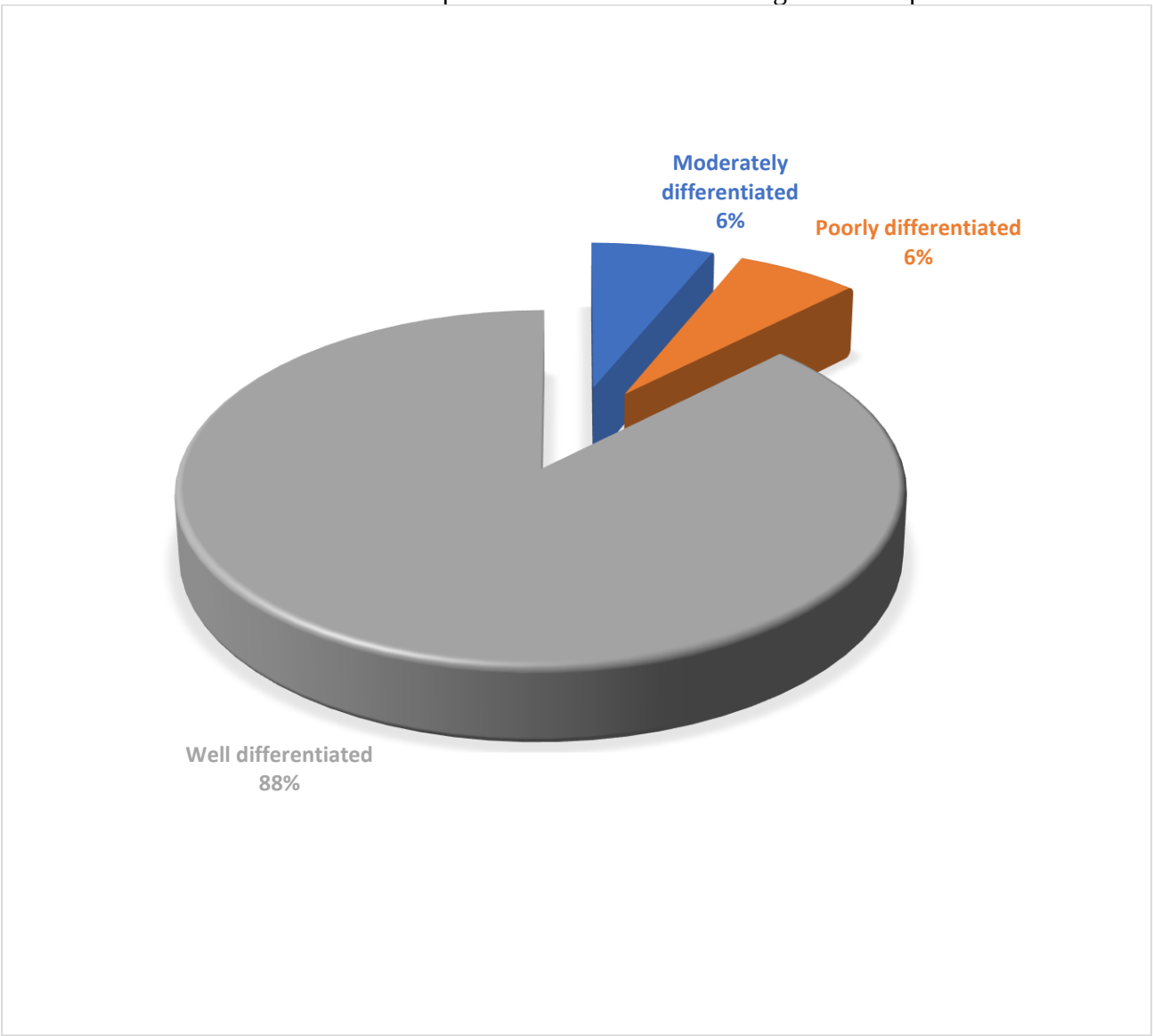

Table 21 Distribution of cTumor staging

cT Staging	Frequency	Percent
Tis	0	0%
T1	3	9.3%
T2	17	53.1%
T3	1	3.1%
T4a	10	31.2%
T4b	1	3.1%
Total	32	100.0%

In our study, 17 [53.1%] patients had T2 and 10 [31.2%] patients had T4a.

The value of z is 4.4483. The value of p is < .00001. The result is significant at p < .05.

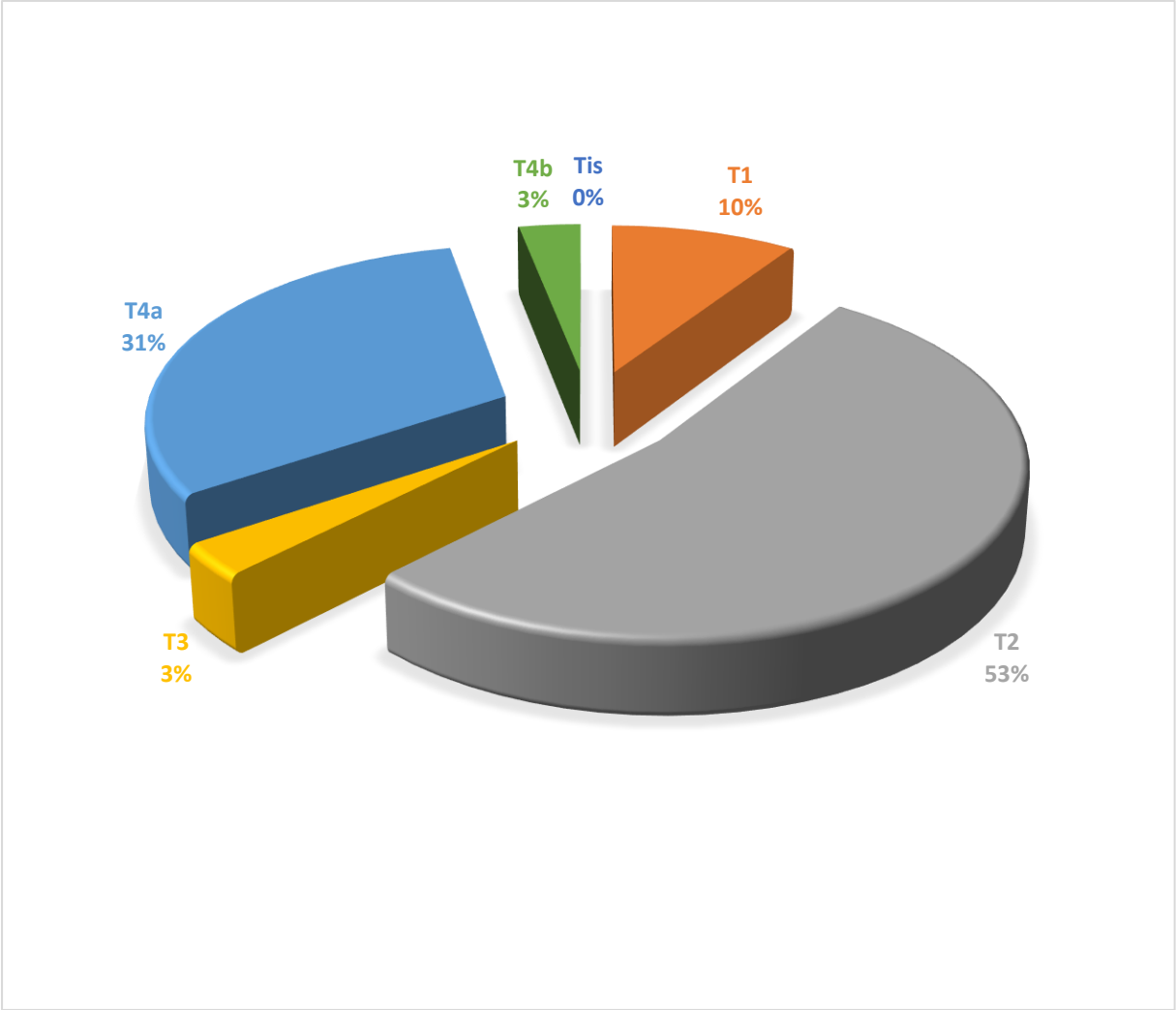

Table 22 Distribution of cNodal staging

cN Staging	Frequency	Percent
N0	**1**	**3.1%**
N1	**11**	**34.3%**
N2a	**6**	**18.7%**
N2b	**12**	**37.5%**
N2c	**1**	**3.1%**
N3	**1**	**3.1%**
Total	**32**	**100.0%**

In our study ,11 [34.3%] patients had N1and 37.5 [55.0%] patients had N2b.

The value of z is 3.4176. The value of p is .00062. The result is significant at p < .05.

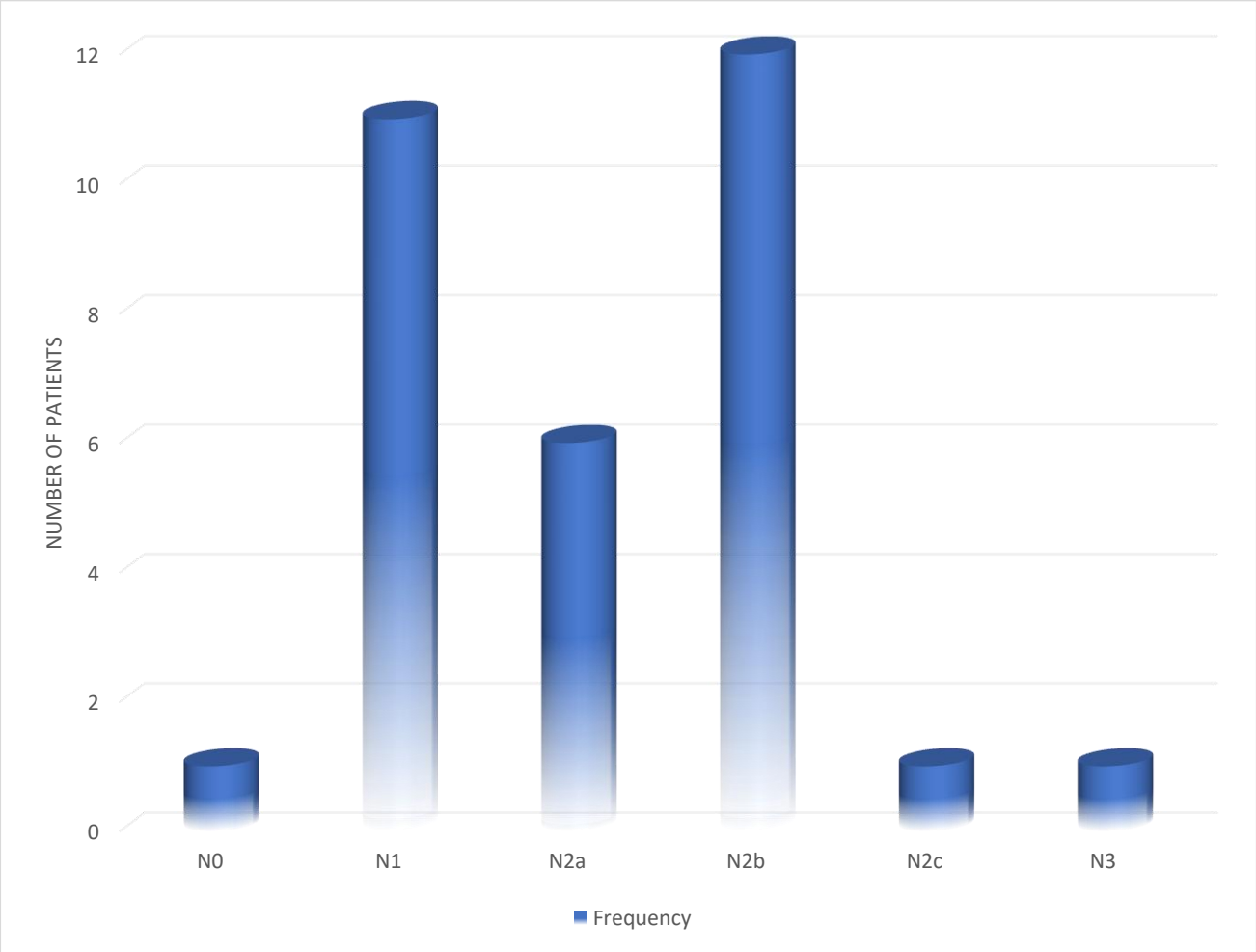

Table 23 Distribution of cM Staging

cM Staging	Frequency	Percent
M0	32	100%
M1	0	0%
Total	32	100.0%

In our study,32 [100.0%] patients had M0.

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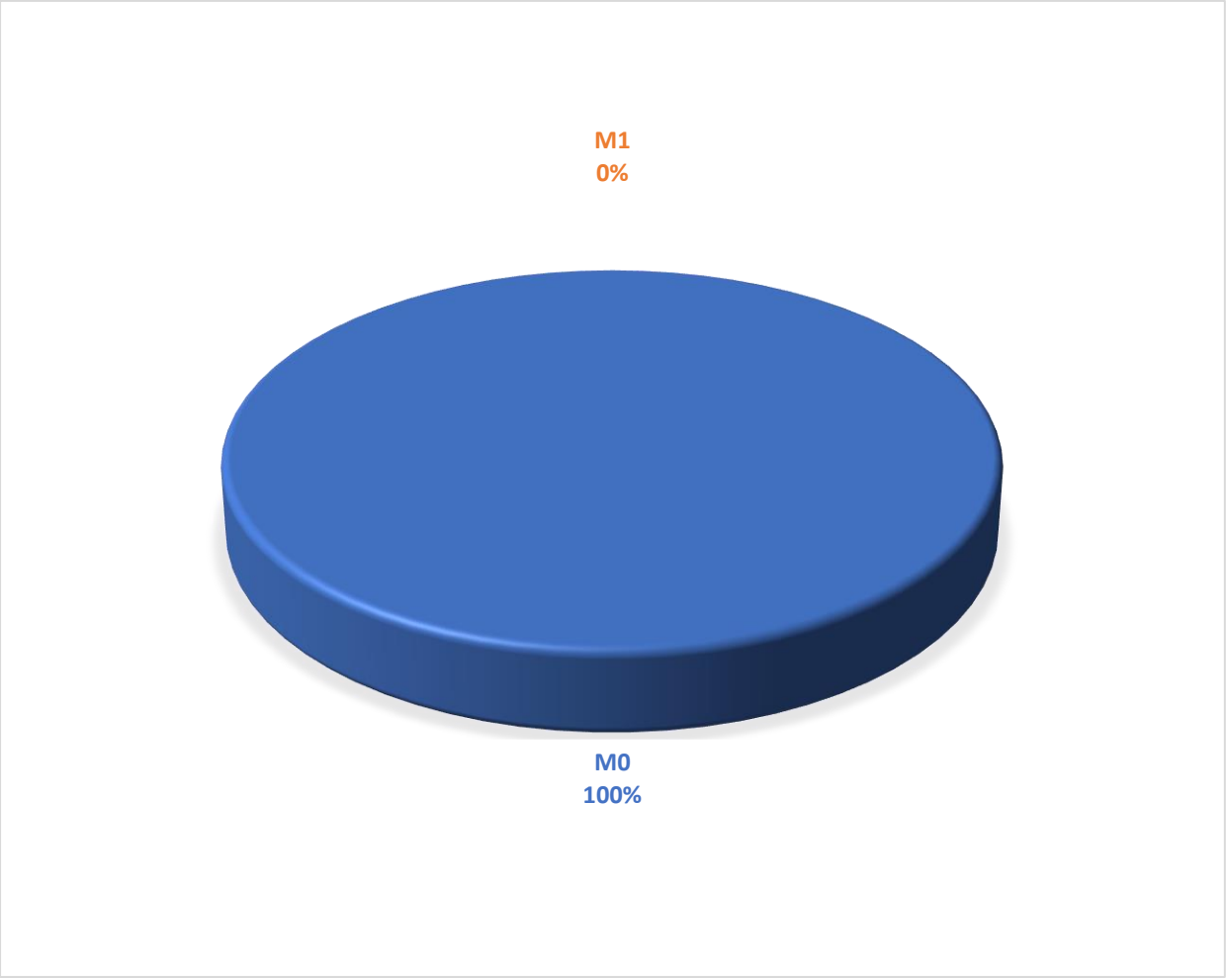


Table 24 Distribution of Staging

Staging	Frequency	Percent
Stage 3	9	28.1%
Stage 4a	22	68.8%
Stage 4B	1	3.1%
Total	32	100.0%

In our study ,22 [68.8%] patients had Stage 4a.

The value of z is 5.4708. The value of p is < .00001. The result is significant at p < .05.

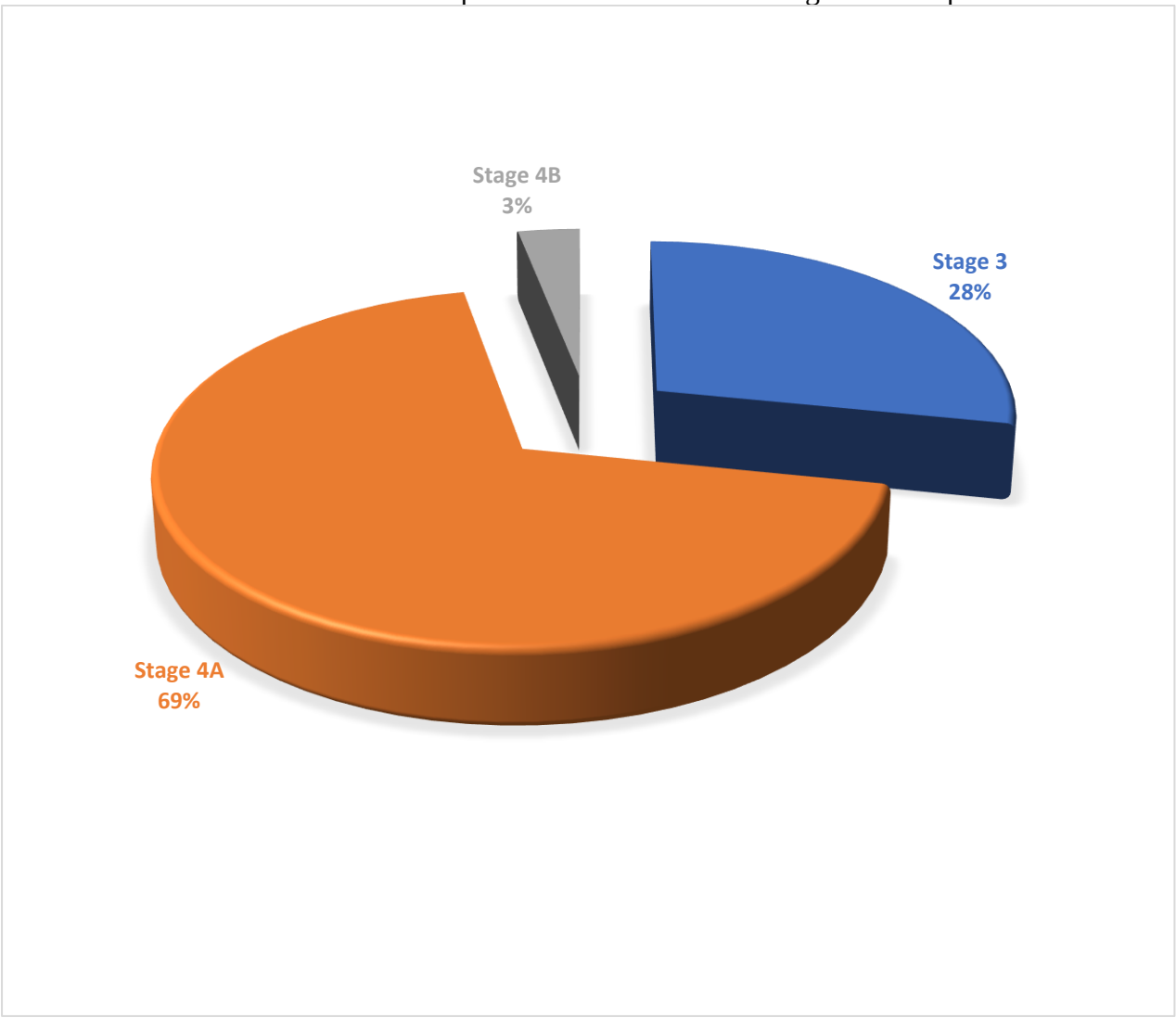


Table 25 Distribution of Surgical Treatment

Surgical Treatment	Frequency	Percent
No	8	25.0%
Yes	24	75.0%
Total	32	100.0%

In our study ,24 [75.0%] patients had Surgical Treatment.

The value of z is 4. The value of p is .00006. The result is significant at p < .05.

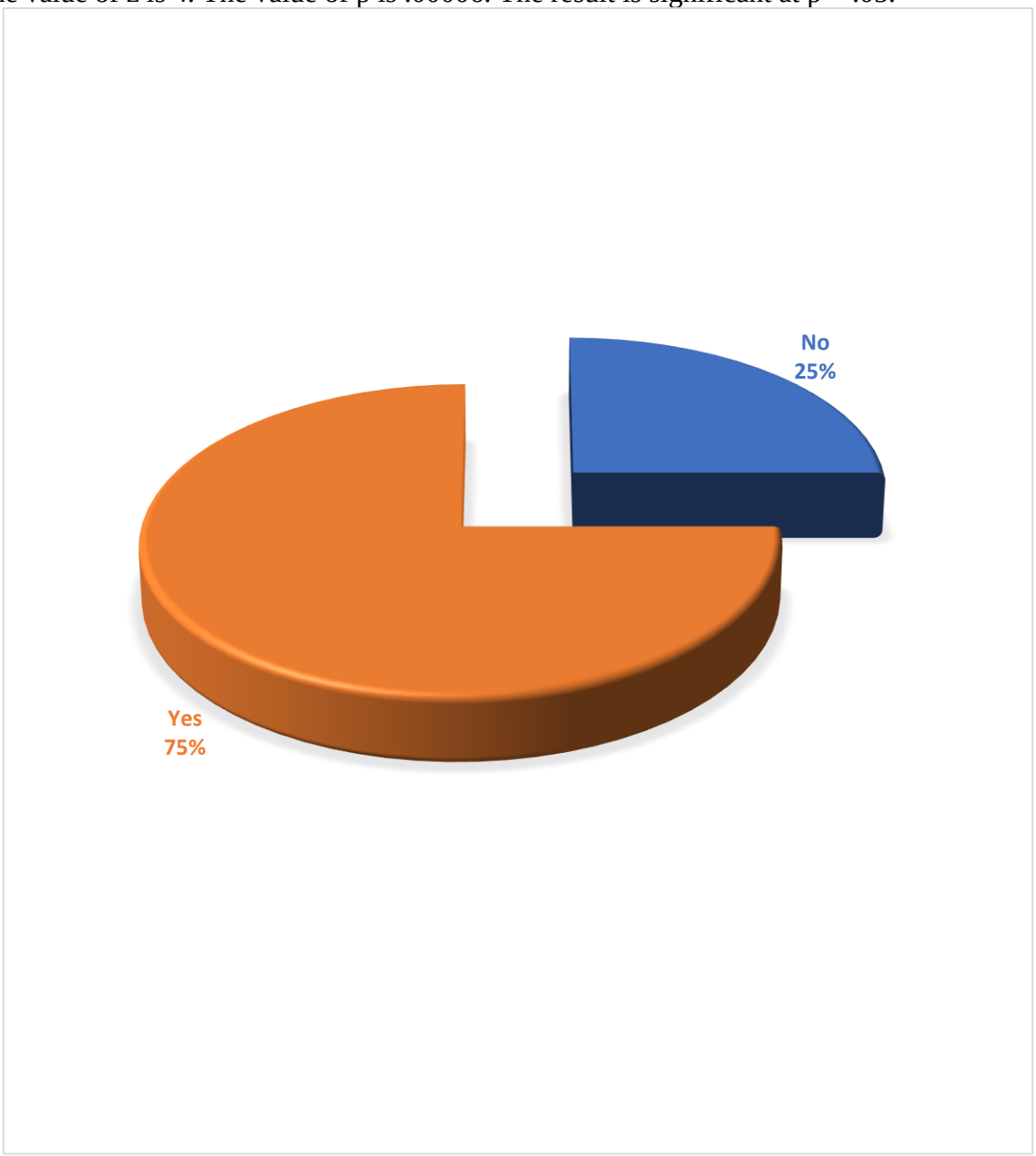


Table 26 Distribution of Chemo therapy

Chemo therapy	Frequency	Percent
No	22	68.8%
Yes	10	31.3%
Total	32	100.0%

In our study ,10 [31.3%] patients had Chemo therapy.

The value of z is 3. The value of p is .0027. The result is significant at p < .05.

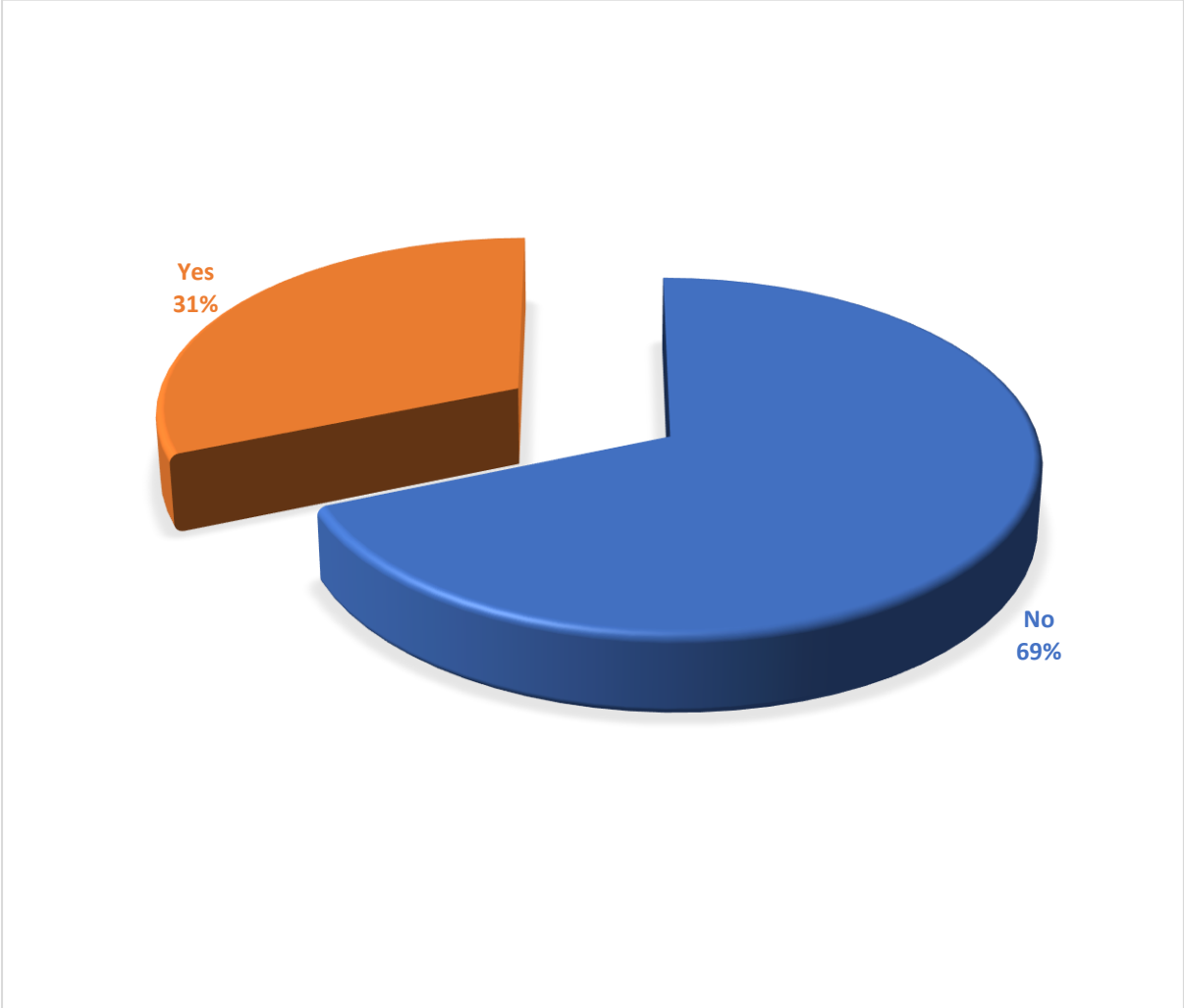


Table 27 Distribution of Radiation therapy

Radiation therapy	Frequency	Percent
No	19	59.4%
Yes	13	40.6%
Total	32	100.0%

In our study,13 [40.6%] patients had Radiation therapy**.**

The value of z is 1.5. The value of p is .13362. The result is not significant at p < .05.

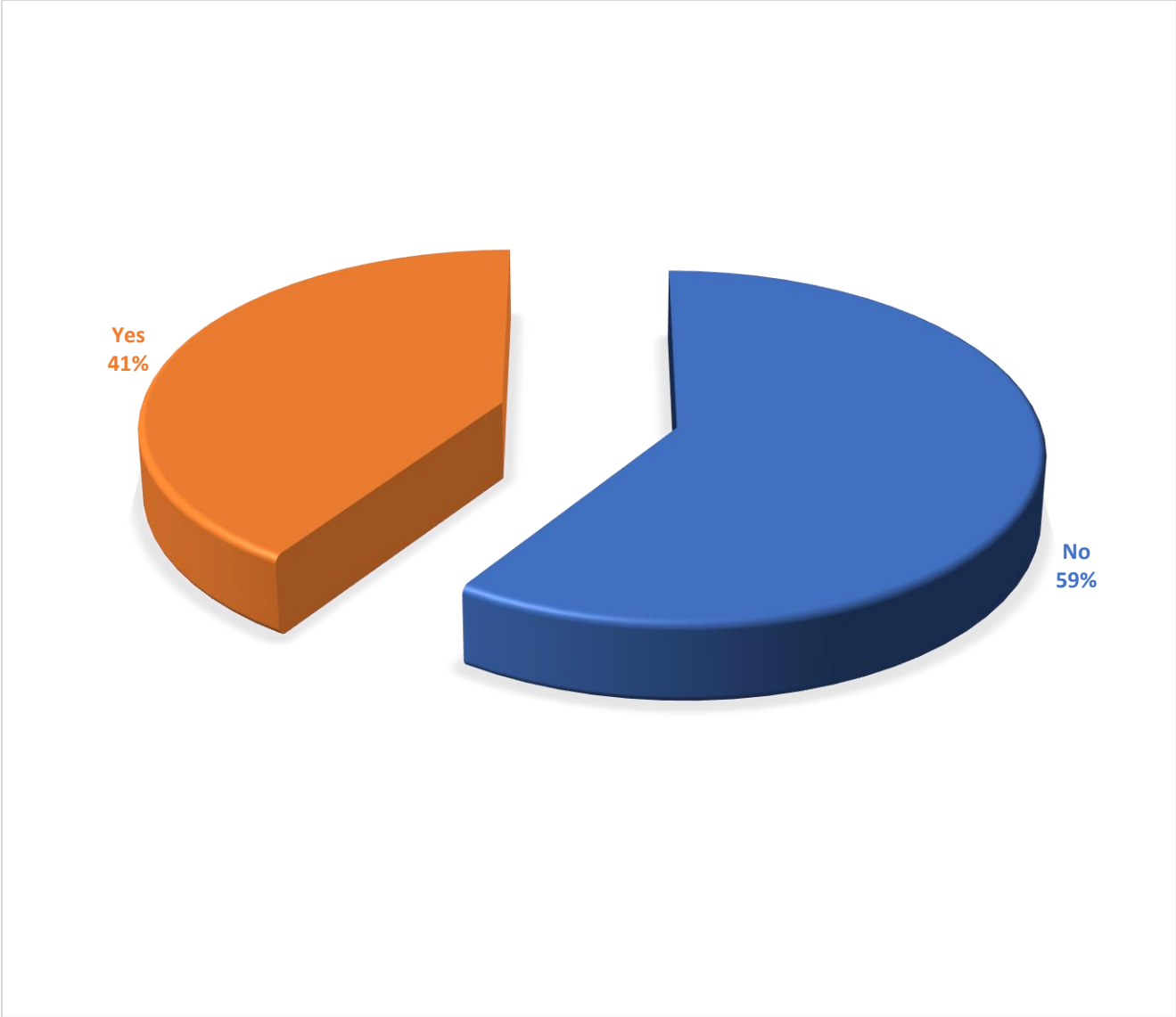


Table 28 Distribution of Palliative

Palliative	Frequency	Percent
No	28	87.5%
Yes	4	12.5%
Total	32	100.0%

In our study ,4 [12.1%] patients had Palliative.

The value of z is 6. The value of p is < .00001. The result is significant at p < .05.

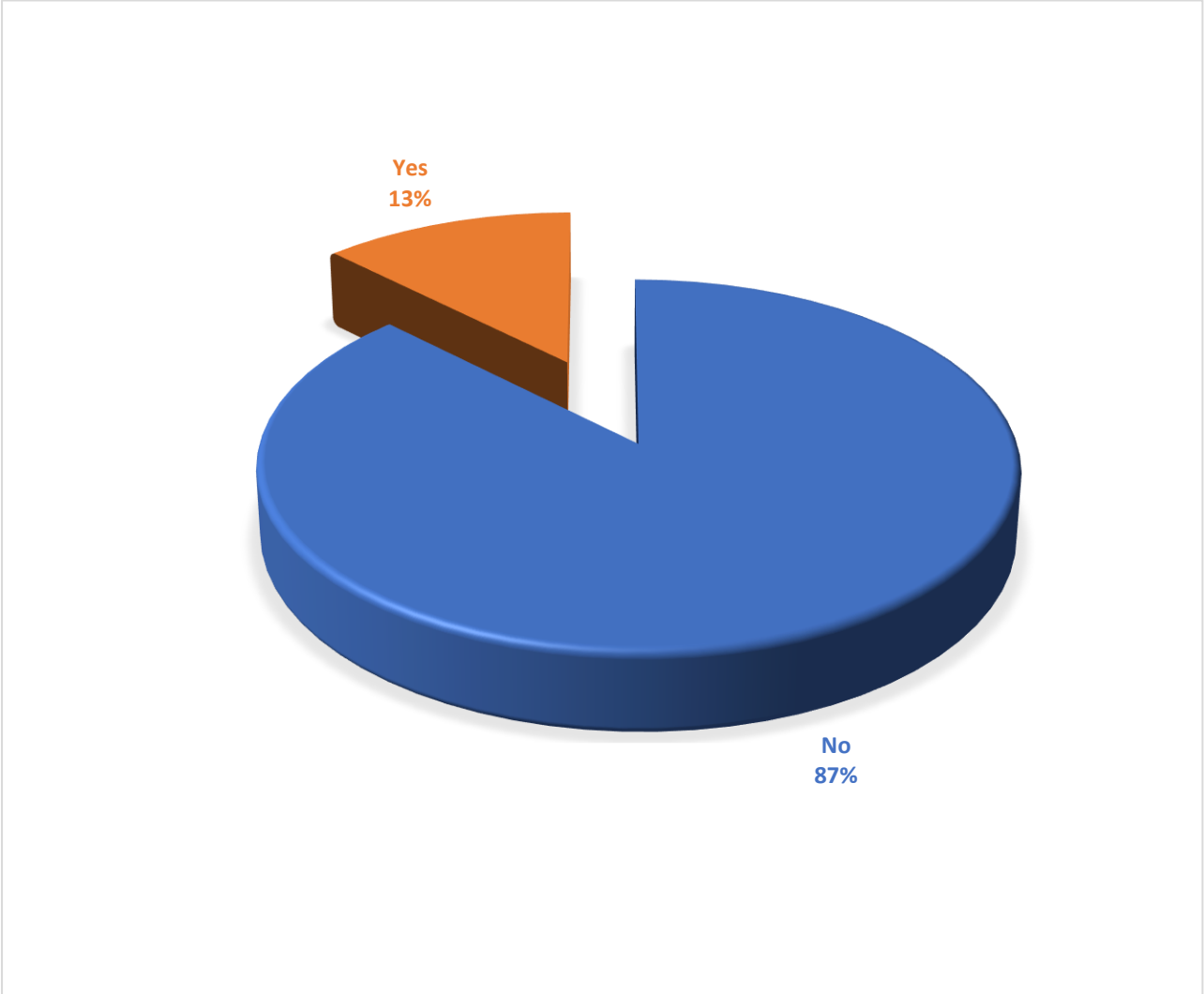


Table 29 Distribution of Complications

Complications	Frequency	Percent
Hematoma	1	3.1%
Nil	30	93.8%
SSI	1	3.1%
Total	32	100.0%

In our study ,1 [3.1%] patient had Hematoma and 1 [3.1%] patient had SSI.

The value of z is 7.5. The value of p is < .00001. The result is significant at p < .05.

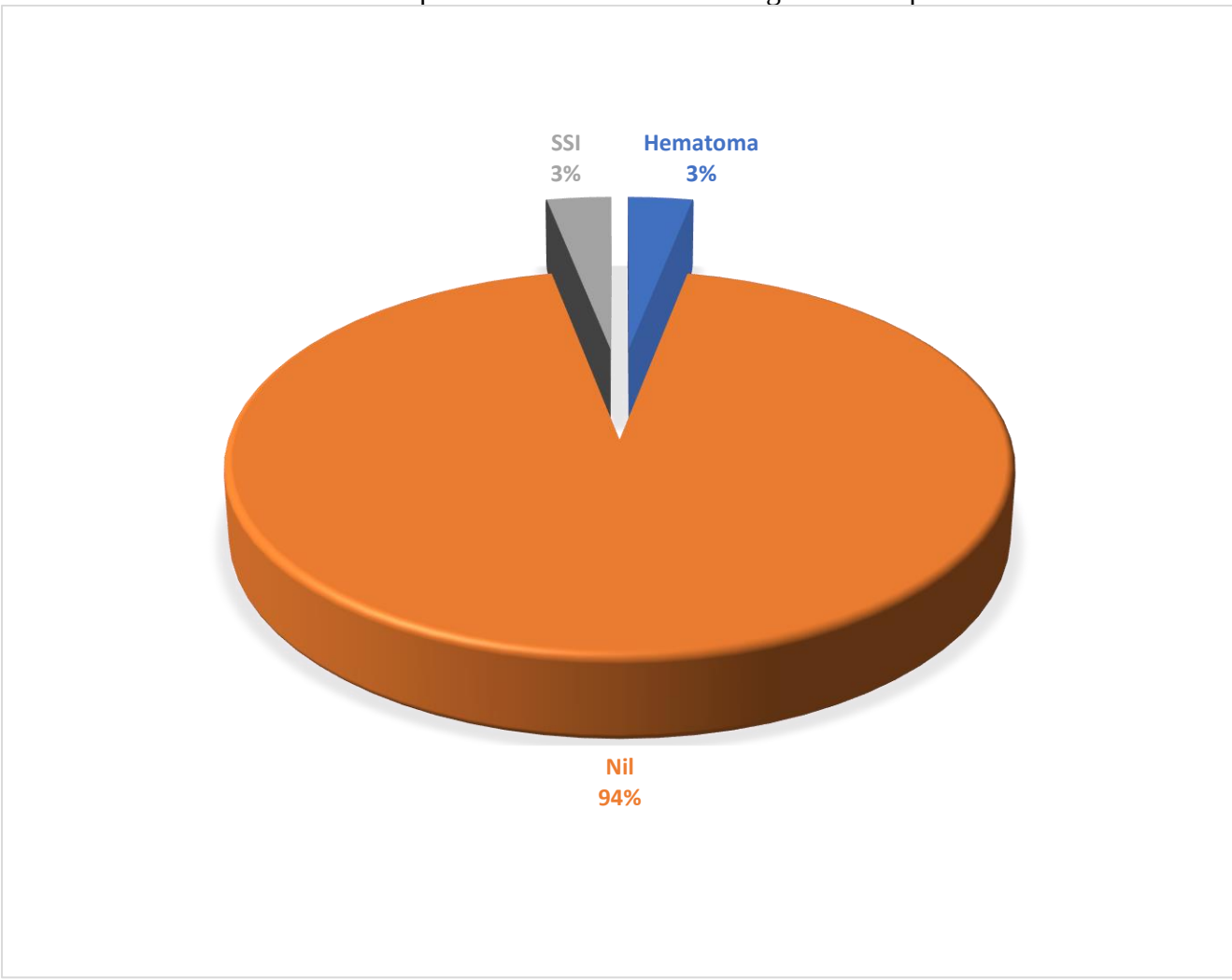
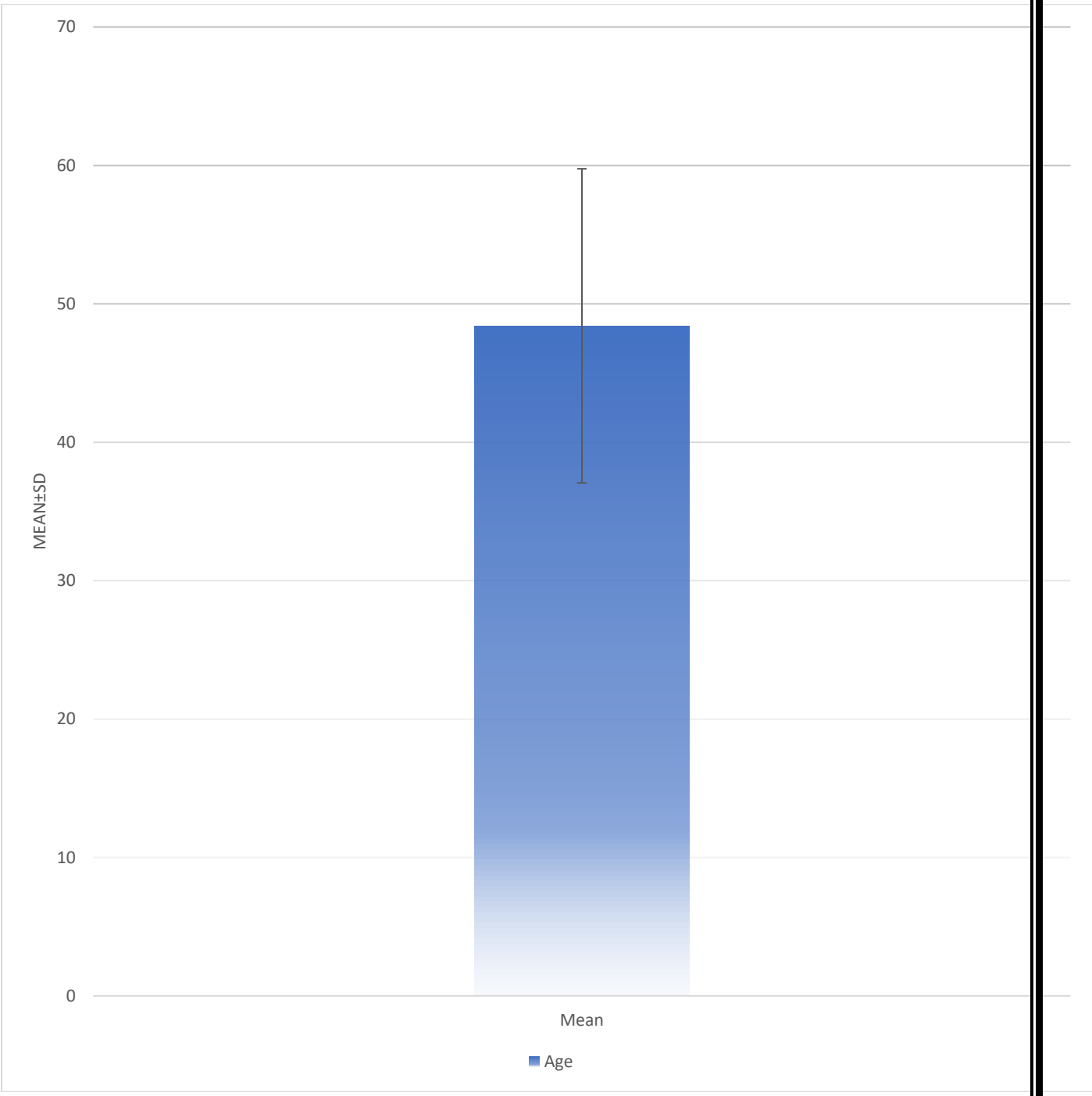


Table 30 Distribution of mean age

	Number	Mean	SD	Minimum	Maximum	Median
age	**32**	**48.4063**	**11.3475**	**26.0000**	**70.0000**	**45.5000**

In above table showed that the mean age [mean±s.d.] of patients was 48.4063± 11.3475.



DISCUSSION

DISCUSSION

The aim of the study was to evaluate the clinicopathological features, risk factors, management and outcome in cases of squamous cell carcinoma of oral cavity in a group of Indian population.

It should be noted primarly that the study period and the population was small upon which interpretation was difficult. Despite those, the study had come up with significant findings upon the variables put forward and multiple variables showed significant results which were worth being noted. Many of the variables and results showed similarities to prior research and for those which did not, it was much more interesting to speculate why.

We had a total of 32 patients for our study during the study period of 1 year from July 2021 – June 2022. Those patients who full filled the inclusion and exclusion criteria was taken in for study purpose according to the methodology. Our study was a cross-sectional study conducted at Santosh Medical college and hospitals.

Out of 32 patients, most of the patients were within the age of 40-49years (11[34.3%]) which was statistically significant [p.00138] [Z=3.2026] followed by 50-59years (7[21.8%]) followed by 30-39years and 60-69years with equal share of 6 patients with 18.7%. Our study inferred that the incidence of oral cavity squamous cell carcinoma was more in the middle age group with maximum at the 4th decade of life followed by the 5th decade. Very few patients were seen in the younger age groups at the 2nd and 3rd decades. We found that, the mean Age of patients was [48.4063± 11.3475]. [53]

According to Padma R *et al*[37], the mean age group of all participants in their study was 54.16 ± 17.25 years ranging from 21-88 years age group. Ampur OY *et al* [32], has studied a total of 50 patients of oral squamous cell carcinoma which ranges from age 33 to 89 years with mean age of 64.24 ±12.01 years. Dhanuthai *et al*[53] had studied a larger population of 6151 cases, mean age of the patients was 58.37±15.77 years. These were suggestive of a further decline in the age of presentation of the disease in the current population which is alarming as in much younger population is being diagnosed in recent studies as ours.

In our study, male population (26 [81.3%]) were higher than the female population(6 [18.8%]) which was statistically significant (p< .00001) (Z=5) with a ratio of 4.22:1. In general females are less prone to the incidence of oral carcinoma due to consumption of tobacco is considerably more in men compared to women.

In our study, 80.7% of total men had habit of smoking where as 92.3% of males have chewing tobacco or tobacco/areca nut containing products as habits. Compared to the male population, 33.3% of females of our study have habituation of smoking whereas, 66.6% of total females have chewing tobacco or tobacco/ areca nut products as their habituation. This shows the significant association of chewing tobacco or areca nut products are more in both genders compared to smoking. Also signifies the major share of tobacco consumption in both genders are for chewing tobacco than smoking tobacco. But it fails to comment between whether the causative factor is areca nut or tobacco in those consuming chewable as both are at times taken together or independently which are highly unlikely to delineate in our study.

In a study conducted by Singh MP *et al* [31] had observed relatively similar results with 75.9% of males and 24.1% females showing male to female ratio of 3:1. Mean age of females were found to be significantly higher in their study. In their study, higher prevalence were there in males consuming smokeless tobacco at 45.0% followed by people with habit of smoking at 41.8%. Whereas in females highest prevalence was in smokeless tobacco users accounting for 72.8%.

According to Pires FR *et al*[28], a mean of 67% of total study subjects were males compared to 33% females. Siriwardeana BS *et al*[44] had observed that a similar male to female ratio of 4:1 conducted in srilanka. Halifa Ndayisabye et al had observed in his study conducted in an eastern African country that male to female ratio was 1.2:1 suggested the variation with the race and location also compared to the south Asian countries. [54]

In our study, all of patients presented to the OPDs with complaints of ulcer (32 [100.0%]) in the oral cavity followed ($p < .00001$)($Z=7.7538$). It was followed by swelling in 15 patients (46.8%), bleeding per oral (9[28.1%]) and trismus in (7[21.8%]). Many other constitutional symptoms were also present at time of presentation of patient to the opd like loose tooth, pain, ear pain, dysphagia/ odynophagia. Many a number of studies have suggested ulcer along with pain alone as the presenting complaints followed by swelling with other constitutional symptoms and also symptoms like ulcer, trismus, bleeding per oral etc. Presenting complaints depends generally on the subsite like, those in buccal mucosa presents with ulcer along with swelling more on the cheek and bleeding per oral whereas those presenting with tongue carcinoma presents with ulcer with or without bleeding per oral. Swellings are otherwise present in the neck in those with clinically palpable lymphnodes.

We also found that, most of the patients had no significant past history [23 [71.9%]] it was statistically significant [p< .00001] [Z=5.6804]. Many studies had suggested correlation with past history of head and neck carcinoma, HPV infections having association with the occurance of oral cavity carcinoma. None of our study subjects had relevant past history but was having diabetes mellitus in 21.8% and hypertension in 6.3% patients.

Studies have suggested many a times recurrence associated with oral carcinoma in those who already had a primary which had undergone treatment in the past. Also in those who have prior HPV infection detected are highly likely to develop head and neck carcinomas especially oral carcinoma in the later life. [(43)] As per our study, none of the patients had any such past histories or even any notable history of HPV infection. General comorbid conditions like diabetes mellitus, hypertension etc doesn't have any significant correlation with oral carcinoma as they possess no threat in incidence of the oral carcinomas. No significant family history was identified in any of the patients. [(55)]

In our study, more number of patients had (28 [87.5%]) Chewing Tobacco which was statistically significant (p< .00001) (Z=6.7799) followed by smoking (23 [71.8%]) and alcohol (11[34.3%]). Results were suggestive and significant enough to justify the most cases being diagnosed in case of those having chewable tobacco. In our Indian setup, most of the patient had habits of chewing tobacco or tobacco containing products like paan as it is an economical way of tobacco addiction compared to high priced cigarettes or cigars. People are consuming tobacco as well as areca nut either individually or together. Hence its unlikely to differentiate the causative factor in oral carcinoma in such cases as both are having carcinogens which may act synergistically. Male to female prevalence in smoking and smokeless tobacco consumption is already mentioned in the above pages under gender classification.

Alcohol being another entity which is found to be a causative factor in oral carcinoma is seen to be in nearly 34.3% of cases and all the cases had consumption of tobacco in either of the ways. So we can conclude whether alcohol alone be a cause for the oral carcinoma but can conclude as it has synergistic effect when consumed along with tobacco as nearly as 20times to those who don't consume alcohol.

Those who consume tobacco in either forms with alcohol presented with higher nodal stages indicating severity of the condition which substantially agrees on its synergistic effect. One case out of the 32 total cases were found to be having broken teeth as the risk factor as the

patient was having chronic trauma to the buccal mucosa with the same teeth and later developed into oral carcinoma.

Anwar N *et al*[43]also justified habituation of chewable tobacco is attributable for carcinoma of oral cavity with more than 2-4 times than non-tobacco chewers. Nearly 77.4% cases where associated with habits of chewing tobacco whereas only 22% cases attributed for smoking. On which more of male patients were associated with tobacco chewing which showed similar results in our study.

Durrani S *et al* [41] observed similar result in their study with 58% patient having chewing tobacco habits in the form of shamma which is local form of tobacco like paan in india. Farrag A *et al*[38], acharya s *et al*[26], showed similar association with chewable tobacco more than non-chewers.

Acharya s *et al*(26) has conducted a study in the indian population collecting datas in the young population per se and came to a conclusion of higher percentage of patients who consumes SLT in various forms belongs to younger age group compared to the older age group which in later life leading to oral carcinomas.

Our study gave a conclusion regarding the premalignant lesions in patients as leukoplakia (9[28.1%]), Erythroplakia (2 [6.3%]) it was statistically significant (p< .00001) (Z=4.9498). Even when leukoplakia seems to be much more common, those with erythroplakia had the worse outcome of them both as those with erythroplakia had developed poorly differentiated (100%) carcinoma which carries worse prognosis as well as there presentation was in a much advanced stage. Anil K Chaturvedi et al also concludes the incidence of oral carcinoma in those with leukoplakia. In both erythroplakia and leukoplakia, there were 100% association with tobacco in either form. Both erythroplakia and leukoplakia showed very small association with those consuming alcohol at 36.3%. This corresponds with the results of Chaturvedi *et al*.(56)Akash N *et al* (52) had come up with a net prevalence of 7.84% of leukoplakia in their study.

In our study, more number of patients had (18 [56.2%]) Buccal Mucosa it was statistically significant (p<.00001) (Z=4.6511) followed by tongue (9[28.1%]), retromolar trigone (5[15.6%]), gingivo buccal sulcus (3[9.3%]), floor of mouth (2[6.2%]), mucosal lip (2[6.2%]), hard palate (2[6.2%]). Jerjes W *et al* [24] observed more case occurring in sites like tongue, floor

of mouth, buccal mucosa and alveolus respectively which is contradicting our study as in ours buccal mucosa is more prevalent.

Pires FR *et al* [28] evaluated lateral border of tongue at 37% as the commonest subsite of presentation followed by alveolar mucosa/ gingiva at 20%, floor of mouth at 19%. Singh MP *et al* [31] showed buccal mucosa and gingiva buccal sulcus as commonest subsite. Ampur OY *et al*[32] suggested lower lip as the commonest site of cancer at 52% followed by tongue at 26%. Padma R *et al*[37] study showed buccal mucosa as the commonest subsite at 49.5%. Farrag A *et al*[38] suggested oral tongue as commonest primary site with 50.6% followed by alveolar ridge (16.1%) floor of mouth (11.5%). Siriwardena BS *et al*[44] showed tongue as the commonest site with 41% followed by buccal mucosa at 37.5% and alveolar mucosa at 25%. Pallavi 0K *et al* [51] found oral tongue carcinoma as commonest at 40% of intra oral carcinoma.

Many a number of studies have already been conducted site specific and various correlation according to the race, countries, risk factors, there been different pattern of subsite prevalence in oral carcinoma. In the western or the developing countries or even in the middle eastern countries, it is suggested that oral tongue is the commonest carcinoma subsite whereas more of Indian studies have concluded buccal mucosa being the commonest subsite for oral carcinoma in Indian population. In our study too the commonest subsite came out to be buccal mucosa which was similar to those studies done in the Indian subcontinent. There are association of buccal mucosa being more prevalent in Indian subcontinent as due to more of tobacco chewing and its forms that are being consumed and the site they used to load the tobacco products in the oral cavity being the buccal mucosa which leaves maximum time of direct contact with the tobacco product.

Less number of patients had (8 [25.0%]) USG Primary Lesion, USG Neck which was statistically significant (p.00006) (Z=4) as many patients came with ulceration as local symptom and those with swelling and neck nodes were the ones who had done USG of the primary lesion and neck. Also many a number of cases presented in advanced stages.

All patients had undergone further radiological imaging before final staging and starting on the treatment. CECT face and neck was the investigation of choice for head and neck carcinoma. Almost all the cases except those diagnosed/ suspected carcinoma of tongue had undergone CECT face and neck following renal function test. There was 71.8% patient who had undergone CECT face and neck. Those patients with suspected or clinically proven cases of carcinoma tongue were done with MRI. In our study, 28.1% cases were done with MRI as they

were diagnosed clinically with carcinoma of tongue. Both MRI and CECT was the imaging modalities of choice according to the subsite and it was an aid in the treatment plan taking into consideration of the extend and invasion of the disease into the adjacent structures. Rest in our study, less number of patients had done PET Scan (11 [34.4%]) which was statistically significant [p.00006] [Z=4] as it was done in those cases those were advanced and also those planned for CCRT or post op chemotherapy.

Majority number of patients had well differentiated [28 [87.5%]] it was statistically significant [p< .00001] [Z=6.5127] followed by moderately and poorly differentiated Tumors at 6.3% each. This was having good significance with post op outcome as many hadn't come with signs of recurrence during the study period and also post op complications were also near negligible.

Padma R *et al*[37] had well differentiated carcinoma at 49.5% followed by moderately differentiated at 34.3% and poorly differentiated carcinoma at 16.2% also suggestive of prevalence of well differentiated carcinoma compared to the other two. Pires FR *et al*[28] moderately differentiated carcinoma was prominent at 40% followed by well differentiated carcinoma at 28% followed by poorly differentiated at 21%.

More number of patients under TNM staging had T2 [17 [53.1%]], followed by T4a [10[31.2%]] and T1 [3[9.3%]] value of z is 4.4483. The value of p is < .00001 and is significant. Nodal staging was done resulted in N1 [11[34.3%]], N2b [12[37.5%]], N2a [6[18.7%]] which was statistically significant [p.00062] [Z=3.4176]. All cases were evaluated for metastasis clinically and radiologically [32 [100.0%]] M0 in TNM Staging.

General staging was analysed as stage 4a [22[68.8%]], stage 3 [9[28.1%]] and stage 4b [1[3.1%]]. The value of z is 5.4708. The value of p is < .00001. All cases were diagnosed in the advanced stage. Jerjes W *et al* [24] concluded after their study that most cases presented in the early stages at T1 N0 and T2 N0. Padma R *et al*[37] suggested 85% advanced clinical stage [stage 3&4] and 15%of early stage [stage 1&2]. Farrag A *et al*[38] showed 2/3rd of the cases [66.6%] as advanced stage whereas 1/3rd cases were early stages [33.3%]. Nobrega TD *et al* [39] showed patient being diagnosed with advanced stages 3&4 tumors at 69.2%.

Improved survival was attributable to early stage diagnosis with negative lymph mets at time of diagnosis where as late stage will inversely affect patient survival. Previously there has been significant amount of cases presenting in the advanced stages due to lack of awareness as well

as management modalities. In the current scenario, more of early stages are being diagnosed which gives better prognosis with less likely chance for recurrence in the later life.

We observed that, higher number of patients had surgical treatment [24 [75.0%]] which was statistically significant [p.00006] [Z=4]. 34.3% had done surgery alone and not radiotherapy. Type of surgery done was based on the extend and site of tumor in the oral cavity. In cases of buccal mucosa, retromolar trigone, gingiva, the option of hemi and segmental mandibulectomy was sought according to the extend and infiltrataion of tumors to the mandible/ masseteric muscles, pteryigoid muscle. Lower maxillectomy was sought in cases with superior extension of tumor in cases of hardpalate, upper buccal mucosa tumors. Okuyama K *et al*[46] had stated all the cases of early stages were taken for surgery at which stage 1 and 2 were considered.

For advanced cases, primary resection with neck dissection followed by chemoradiation was done. Durrani S *et al*[41] showed that most of their patient of 73% went to surgery followed by radiotherapy whereas 2% had surgery alone. Padma R *et al*[37] showed 43.4% patients were fit for surgery followed by chemoradiation. Radiation therapy was given to 31.3% of the patients post op in those who had undergone surgery. Montero PH *et al*[30] also suggested multidisciplinary approach with radiationtherapy post operative leads to better survival and surgical success. Jerjes W *et al*(24) suggested all 105 study patients [100%] who presented with early and advanced cases end up in primary resection ± neck dissection and reconstruction when indicated. Out of which 22 patients [20.9%] had availed adjuvant radiotherapy which correlates without study. Post operation, out of those patient undergone surgery 24 [75.0%], only 2 patients had complication as 1 patient developed surgical site infection and another patient developed hematoma. Most of the patients had no [30 [93.8%]] no Complications which was statistically significant [p< .00001] [Z=7.5].

Few numbers of patients whose primary was advanced stage as in stage 4a and 4b and those who had unressectable tumors had been given chemo therapy [10 [31.3%]] which was statistically significant [p.0027] [Z=3] out of which 4 patients [12.5%] received palliative chemotherapy and 4 patients [12.5%] had lost followup post chemotherapy. 4 patients [12.5%] who had unressectable tumors with higher extend of infiltration had ended up in palliative treatment. Those patient who end up with skull base and pan facial spread of tumor are less likely to survive the surgical procedure as it demands compound resection of a major facial anatomical landmarks and vital structure thereby which, these candidates will be subjected to

neoadjuvant chemoradiotherapy and may end up in palliative treatment if they show significantly less response to neoadjuvant chemotherapy.

CONCLUSION

India being one among the developing nations face a serious threat from the rise in the cases of head and neck carcinoma, precisely oral carcinoma. There seems to be decline in the age of onset of disease compared to western nations due to consumption of tobacco products, alcohol in various forms. Its high time to develop a good campaign in promoting to quit the tobacco and alcohol products so as there will be higher chance of survival for middle aged population. Since oral carcinoma can be attributable to low socioeconomic status, awareness and support has to be conducted accordingly.

Newer tendency of HPV causing oral carcinoma is another analogue that has to be considered as it is the commonest cause of head and neck carcinoma in western world. So, promoting vaccination against HPV can help out in reducing the possible occurrence of HPV related oral carcinoma. Study had concluded the early detection of carcinoma in many a number of cases but near equal contribution is from the advanced disease group also. This has to be brought to a significant early presentation state over the next few years of time. Treatment strategies are being successful as the study suggest with far low complications with good aesthetic and functional recovery in post op period.

More of awareness programs are to be initiated in the field of oral carcinoma against the consumption of tobacco products as well as alcohol products which have high association with oral carcinoma in the Indian population where HPV related head and neck carcinoma is not so prevalent compared to western world. More emphasise has to be given in the younger population as occurrence of oral carcinoma is falling into much earlier decades from the previous elderly generation group. Influence of socioeconomic status is another entity to be taken care of as there is high association with low socioeconomic status with consumption of tobacco products as current generation or even the older generation are in search of addictions at more cost effective way that being tobacco products especially chewable tobacco which are more economical than smoking cigarettes. Early detection plays a vital role in post op morbidity and outcome of treatment and has to be made adequate with educating self examination and clinician education for early diagnosis on first visits. This will significantly reduce the advanced stage presentation of disease as described in the study.

SUMMARY

- In our study, out of 32 patients, most of the patients were 40-49 years of age.
- We found that, male population was higher than the female population and male: female ratio was 4.33:1.
- Our study showed that, most of the patients presented with Ulcer, followed by swelling and trismus which was statistically significant. Most of the patients had no Past history.
- Significant number of patients had Chewing Tobacco as their risk factor followed by smoking and alcohol.
- Leukoplakia was found to be in 28.1% cases which shows its more prevalent in oral cavity carcinoma patients.
- Buccal mucosa was found to be the commonest subsite in our study and when compared with other Indian and international studies, those studies in india shares common result whereas those international studies have more result with tongue as the commonest subsite in oral cavity.
- Majority of cases had well differentiated carcinoma with significant and noteworthy.
- A significant number of patients presented with T2 staging followed by T4a with nodal status of N2b being most common followed by N1.
- A significant number of cases were identified with stage 4A carcinoma.
- A significant number of 24 patients went for surgical treatment with or without reconstruction
- A total of 10 patients were treated with radiotherapy followed by their primary surgery.
- Nearly 10 patients were sent for chemotherapy out of which 4 patients are done with palliative chemotherapy.
- Post operative phase of those patient who had under gone surgery had very less complication which was significant.

Figure 23 WLE local excision in progress for Carcinoma of Buccal Mucosa

Figure 24 Plastic surgery reconstruction with PMMC flap in process for Carcinoma of Buccal Mucosa

REFERENCES

REFERENCES

1. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBACAN 2012. *International journal of cancer*. 2015;136(5):e359–e86. 10.1002/ijc.29210
2. Westra WH, Lewis JS. Update from the 4th edition of the world health organization classification of head and neck tumors: oropharynx. *Head neck pathology*. 2017;11(1):41–7. 10.1007/s12105-017-0793-2
3. Ernani V, Saba NF. Oral cavity cancer: risk factors, pathology, and management. *Oncology*. 2015;89(4):187–95. 10.1159/000398801
4. Bhisey RA. Chemistry and toxicology of smokeless tobacco. *Indian journal of cancer*. 2012;49(4):364 10.4103/0019-509x.107735
5. Mitamura, J., Onodera, K., & Ooya, K. (2008). Histopathological and immunohistochemical study of oral lichen planus in the buccal mucosa: relationship between clinicopathological features and histometrical analysis. *Oral Medicine & Pathology*, *13*(1), 1–6. https://doi.org/10.3353/OMP.13.1
6. Gray H et al. *Gray's anatomy: The anatomical basis of clinical practice*. Edinburgh; New york: Elsevier Churchill Livingstone; 2005. 39th edition
7. Moore KL, Dalley AF, Agur AMR. 6th edition. *Clinically oriented anatomy*. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2010.
8. Ross MH, Pawlina W. *Histology: A text and atlas: with correlated cell and molecular biology*. 5th ed. Baltimore, MD: Lippincott Williams & Wilkins; 2006.
9. Ellis GL et al. *Tumors of the salivary glands. AFIP atlas of tumor pathology*. 4th series. Washington, DC: American registry of pathology in collaboration with the armed forces institute of pathology; 2008.
10. Flint PW, Cummings CW. *Cummings otolaryngology--head & neck surgery*. 5th ed. Philadelphia: mosby/elsevier; 2010.
11. Kutler DI, Auerbach AD, Satagopan J, et al. High incidence of head and neck squamous cell carcinoma in patients with fanconi anemia. *Archives of otolaryngology head neck surgery*. 2003;129(1):106–112.

12. Liao CT, Kang CJ, Chang JT, et al. Survival of second and multiple primary tumors in patients with oral cavity squamous cell carcinoma in the betel quid chewing area. *Oral oncology.* 2007;43(8):811–819.
13. Shoaib T, Soutar DS, Macdonald DG, et al. The accuracy of head and neck carcinoma sentinel lymph node biopsy in the clinically N0 neck. *Cancer.* 2001;91(11):2077–2083.
14. Fakih AR, Rao RS, Borges AM, et al. Elective versus therapeutic neck dissection in early carcinoma of the oral tongue. *American journal of surgery.* 1989;158(4):309–313.
15. Gupta PC, Ray CS, Sinha DN, Singh PK. 2011. "Smokeless tobacco: a major public health problem in the sea region: a review." Indian journal of public health 55 (3): 199–209.
16. Lucenteforte E, Garavello W, Bosetti C, LA V C. 2009. "Dietary factors and oral and pharyngeal cancer risk." Oral oncology 45 (6): 461–67.
17. Chainani-wu N, Epstein J, Touger-decker R. 2011. "Diet and prevention of oral cancer: strategies for clinical practice." Journal of the American Dental Association 142 (2): 166–69.
18. Harty IC, Caporaso N E, Hayes R B, Winn D M, Bravo-otero E. And others. 1997. "Alcohol dehydrogenase 3 genotype and risk of oral cavity and pharyngeal cancers." Journal of the national cancer institute 89 (22): 1698–705.
19. Fernandez G L, Sankaranarayanan R, Anta J J Lence, Rodriguez S A, Parkin D M. 1995. "An evaluation of the oral cancer control program in cuba." Epidemiology 6 (4): 428–31.
20. Mathew B, Sankaranarayanan R, Sunilkumar K B, Kuruvila B, Pisani P. And others. 1997. "Reproducibility and validity of oral visual inspection by trained health workers in the detection of oral precancer and cancer." British journal of cancer 76 (3): 390–94.
21. Ross GL, Shoaib T, Soutar DS, et al. The first international conference on sentinel node biopsy in mucosal head and neck cancer and adoption of a multicenter trial protocol. *Annuls of surgical oncology.* 2002;9(4):406–410.
22. Bartelink H, Breur K, Hart G, et al. The value of postoperative radiotherapy as an adjuvant to radical neck dissection. *Cancer.* 1983;52(6):1008–1013
23. Woolgar J A. 2006. "Histopathological prognosticators in oral and oropharyngeal squamous cell carcinoma." Oral oncology 42 (3): 229–39.

24. Jerjes W, Upile T, Petrie A, Riskalla A, Hamdoon Z, Yourvachis M, Karavidas K, Jay A, Sandison A, Thomas GJ, Kalavrezos N. Research clinicopathological parameters, recurrence, locoregional and distant metastasis in 115 t1-t2 oral squamous cell carcinoma patients.2010
25. Trotta BM, Pease CS, Rasamny JJ, Raghavan P, Mukherjee S. Oral cavity and oropharyngeal squamous cell cancer: key imaging findings for staging and treatment planning. Radiographics. 2011 mar;31(2):339-54.
26. Acharya S, Tayaar AS. Analysis of clinical and histopathological profiles of oral squamous cell carcinoma in young indian adults: a retrospective study. Journal of dental sciences. 2012 sep 1;7(3):224-30.
27. Sadasivan A, Thankappan K, Rajapurkar M, Shetty S, Sreehari S, Iyer S. Verrucous lesions of the oral cavity treated with surgery: analysis of clinico-pathologic features and outcome. Contemporary clinical dentistry. 2012 jan;3(1):60.
28. Pires FR, Ramos AB, Oliveira JB, Tavares AS, Luz PS, Santos TC. Oral squamous cell carcinoma: clinicopathological features from 346 cases from a single oral pathology service during an 8-year period. Journal of applied oral science. 2013 sep;21:460-7.
29. Jadhav KB Gupta N. Clinicopathological prognostic implicators of oral squamous cell carcinoma: need to understand and revise. North american journal of medical sciences. 2013 dec;5(12):671.
30. Montero PH, Patel SG. Cancer of the oral cavity. Surgical oncology clinics. 2015 jul 1;24(3):491-508.
31. Singh MP, Kumar V, Agarwal A, Kumar R, Bhatt ML, Misra S. Clinico-epidemiological study of oral squamous cell carcinoma: a tertiary care centre study in north india. Journal of oral biology and craniofacial research. 2016 jan 1;6(1):32-5.
32. Ampur OY, Sudarsa IW, Suryawisesa IB. P16 expression correlation with clinicopathological features of oral cavity squamous cell carcinoma patients in bali. Bali medical journal. 2016 may 31;5(3):362-6.
33. Peng Q, Wang Y, Quan H, Li Y, Yang Z. Oral verrucous carcinoma: from multifactorial etiology to diverse treatment regimens. International journal of oncology. 2016 jul 1;49(1):59-73.
34. Jin X, Liu D, Zhao X, Zhou Y, Jiang L, Li J, Zeng X, Chen Q. Analysis of clinicopathological characteristics associated with the outcome of oral squamous cell

carcinoma and the establishment of tissue microarrays. Oncology letters. 2016 nov 1;12(5):3175-82.

35. Feng Z, Xu QS, Wang C, Li B, Li JZ, Mao MH, Li H, Qin LZ, Han Z. Clinicopathological features, management and outcome of patients with poorly-differentiated oral and oropharyngeal squamous cell carcinoma. Journal of cranio-maxillofacial surgery. 2017 sep 1;45(9):1478-85.
36. Majumdar B, Patil S, Sarode SC, Sarode GS, Rao RS. Clinico-pathological prognosticators in oral squamous cell carcinoma: an update. Translational research in oral oncology. 2017 nov 6;2:2057178x17738912.
37. Padma R, Paulraj S, Sundaresan S. Squamous cell carcinoma of buccal mucosa: prevalence of clinicopathological pattern and its implications for treatment. SRM journal of research in dental sciences. 2017 jan 1;8(1):9.
38. Farrag A, Shaukat A, Ali M, Kandil M. Clinico-pathological features and outcome of treat-ment of saudi patients with oral cavity cancer: a single institutional experience. International journal of oncology res. 2018;1(006).
39. Nóbrega TD, Pereira-pinto L, De Souza LB. Clinicopathological evaluation and survival of patients with squamous cell carcinoma of the tongue. Medicina oral, patologia oral y cirugia bucal. 2018 sep;23(5):e579.
40. Liu T, David M, Ellis O, Low TH, Palme CE, Clark J, Batstone M. Treatment for oral squamous cell carcinoma: impact of surgeon volume on survival. Oral oncology. 2019 sep 1;96:60-5.
41. Durrani S, Al-dhahari S, Sebeih S, Wani T, Al Qahatani K, Heena H. Clinical characteristics of head and neck cancers at a tertiary care hospital. Population medicine. 2020 apr 30;2(april).
42. Borse V, Konwar AN, Buragohain P. Oral cancer diagnosis and perspectives in india. Sensors international. 2020 jan 1;1:100046.
43. Anwar N, Pervez S, Chundriger Q, Awan S, Moatter T, Ali TS. Oral cancer: clinicopathological features and associated risk factors in a high risk population presenting to a major tertiary care center in pakistan. Plos one. 2020 aug 6;15(8):e0236359.
44. Siriwardena BS, Karunathilaka HD, Kumarasiri PV, Tilakaratne WM. Impact of histological and molecular parameters on prognosis of oral squamous cell carcinoma: analysis of 290 cases. Biomed research international. 2020 oct 14;2020.

45. Tseng YJ, Wang HY, Lin TW, Lu JJ, Hsieh CH, Liao CT. Development of a machine learning model for survival risk stratification of patients with advanced oral cancer. Jama network open. 2020 aug 3;3(8):e2011768-.
46. Okuyama K, Yanamoto S, Michi Y, Shibata E, Tsuchiya M, Yokokawa M, Naruse T, Tomioka H, Kuroshima T, Shimamoto H, Ikeda T. Multicenter retrospective analysis of clinicopathological features and prognosis of oral tongue squamous cell carcinoma in adolescent and young adult patients. Medicine. 2021 oct 10;100(41).
47. Yang SW, Lee YS, Chang LC, Yang CH, Luo CM, Wu PW. Oral tongue leukoplakia: analysis of clinicopathological characteristics, treatment outcomes, and factors related to recurrence and malignant transformation. Clinical oral investigations. 2021 jun;25(6):4045-58.
48. Shinohara S, Kikuchi M, Harada H, Hamaguchi K, Asato R, Tamaki H, Mizuta M, Hori R, Kojima T, Honda K, Tsujimura T. Clinicopathological characteristics and survival outcomes of patients with buccal squamous cell carcinoma: results of a multi-institutional study. Medicina. 2021 dec 13;57(12):1361.
49. Chao, T. Y., Chan, L. P., Lee, H. H., Kao, Y. H., Jhong, Y. P., Chiang, C. H., Chuang, S. T., & Huang, C. J. (2021). Is pathological T4a an independent indication of adjuvant therapy in buccal mucosal or gingival squamous cell carcinoma? *Therapeutic Radiology and Oncology*, *5*(0), 12. https://doi.org/10.21037/TRO-21-1
50. Peña-cardelles JF, Moro-rodríguez JE, Cebrián-carretero JL, Pozo-kreilinger JJ. Commentary on "clinicopathological features of programmed cell death-ligand 1 expression in patients with oral squamous cell carcinoma". Open medicine. 2022 jan 1;17(1):227-8.
51. Pallavi, K., Tandon, A., Gulati, N., Juneja, S., & Shetty, D. (2021). Histopathological prognosticators and their clinicopathological correlation in oral squamous cell carcinomas of the tongue. *Journal of Cancer Research and Therapeutics*, *0*(0), 0. https://doi.org/10.4103/JCRT.JCRT_392_20
52. Akash N, A., & Arivarasu, L. (n.d.). Comparison of Prevalence of Leukoplakia in Males and Females among Chennai Population. *Journal of Research in Medical and Dental Science*, *9*(10), 87–91. Retrieved November 15, 2022, from https://www.jrmds.in/articles/comparison-of-prevalence-of-leukoplakia-in-males-and-females-among-chennai-population-86870.html

53. Dhanuthai K, Rojanawatsirivej S, Thosaporn W, Kintarak S, Subarnbhesaj A, Darling M, et al. Oral cancer: a multicenter study. Medicina oral patologia oral cirugia bucal. 2017;0–0.
54. Ndayisabye H, Ndagijimana A, Biracyaza E, Umubyeyi A. Factors associated with oral cancer adverse outcome at the rwanda military hospital, a retrospective cross-sectional study. Frontiers in oral health. 2022 mar 18;0:20.
55. Zaravinos A. An updated overview of HPV-associated head and neck carcinomas. Oncotarget. 2014 jun 30;5(12):3956-69. Doi: 10.18632/oncotarget.1934. PMID: 24970795; PMCID: PMC4147298.
56. Chaturvedi AK, Udaltsova N, Engels EA, Katzel JA, Yanik EL, Katki HA, Lingen MW, Silverberg MJ. Oral leukoplakia and risk of progression to oral cancer: a population-based cohort study. Journal of national cancer institute. 2020 oct 1;112(10):1047-1054. Doi: 10.1093/jnci/djz238. PMID: 31860085; PMCID: PMC7566351.
57. Ma, Y., Xia, R., Ma, X., Judson-Torres, R. L., & Zeng, H. (2021). Mucosal Melanoma: Pathological Evolution, Pathway Dependency and Targeted Therapy. *Frontiers in Oncology*, *11*, 2833.
58. Kreimer AR, Clifford GM, Boyle P, Franceschi S. (2005). Human papillomavirus types in head and neck squamous cell carcinomas worldwide: a systematic review. *Cancer Epidemiol Biomarkers Prev* 14:467-475.
59. Zandberg DP, Bhargava R, Badin S, Cullen KJ. (2013). The role of human papillomavirus in nongenital cancers. *CA Cancer J Clin* 63:57-81.
60. Leemans CR, Braakhuis BJ, Brakenhoff RH. (2011). The molecular biology of head and neck cancer. *Nature Review Cancer* 11: 9-22.
61. Sato T. A study on effect of mechanical irritation in development and progression of tongue cancer. *Kokubyo Gakkai Zasshi.* 1995;62:532–50.
62. Velly AM, Franco EL, Schlecht N, Pintos J, Kowalski LP, Oliveira BV, et al. Relationship between dental factors and risk of upper aerodigestive tract cancer. *Oral Oncology.* 1998;34:284–91
63. Rosenquist K. Risk factors in oral and oropharyngeal squamous cell carcinoma: A population-based case-control study in Southern Sweden. *Swedish Dental Journal Supplement.* 2005;179:1–66

PROFORMA

Date:

Name: Age/Sex:

IPD no: Occupation:

Address:

Socio-economic status:

Final Diagnosis:

Treatment Plan: Date of surgery:

HISTORY

Chief complaints :

History of presenting illness :

Past history :

Family history :

Risk factors :

- Smoking
- Alcohol
- Chewing tobacco
- Snuff dipping
- Dental caries
- HPV
- Syphilis
- Familial predisposition

Premalignant lesion:

- Leukoplakia
- Erythroplakia
- OSMF
- Nicotine stomatitis

EXAMINATION

General physical examination :

PR: BP: Temp: SpO2: RR:

Local examination :

Subsite :

- mucosal lip
- the mandibular alveolus
- floor of mouth
- tongue [anterior two-thirds]
- buccal mucosa
- retromolar trigone
- maxillary alveolus
- hard palate

Systemic examination :

INVESTIGATIONS:

USG [Primary lesion] :

USG [Neck] :

CT Head & Neck :

Histopathological Report

[Wedge biopsy/Punch biopsy] :

Histological type :

- Well differentiated
- Moderately differentiated
- Poorly differentiated

Staging of the Tumor :

<u>Treatment:</u>

Surgical :

Chemo-radiation :

Paliative **:**

SANTOSH MEDICAL COLLEGE AND HOSPITAL [GHAZIABAD]

INFORMED CONSENT

I _____ Son/Daughter/Wife of _____ resident of _____.

hereby declare that I give my full, free and voluntary informed consent in the thesis – **Clinico-pathological features and management in patients with carcinoma of oral cavity – a cross sectional observational study.** Dr._____ has informed me to my full satisfaction, in the language I understand, about the purpose, nature of study and various laboratory investigations for the study to be carried out. I have been informed about the duration of the study and instructions to be followed during the study period.

I give full consent for being enrolled in the above study and I reserve my rights to withdraw from this study, whenever I wish without prejudice of my right to undergo further treatment at Santosh Hospital, Ghaziabad U.P.

Patient's/ Patient's relative's signature
Or thumb impression

Doctor's signature

Name:

Date:

We have witnessed that the patient signed the above form in the presence of his free will after fully understanding its content.

Signature of Witness

Name

Signature of Investigator
Name: Dr. Nithin R Pillai
Designation: PG
Department of General Surgery
Contact No.- 9847388440

संतोष मेडिकल कॉलेज एवं अस्पताल [गाजियाबाद]

<u>सहमति पत्र [सूचित]</u>

मैं _____ बेटा / बेटी /पत्नी_____

निवासी _____ घोषणा करता हूं कि मैं डॉ ._____, ने मुझे मेरी भाषा में अपने अध्ययन **Clinico-pathological features and management in patients with carcinoma of oral cavity – a cross sectional observational study** अध्ययन के उद्देश्य के बारे में, और अध्ययन के दौरान अपनाई जाने वाली विभिन्न प्रयोगशाला जांच के बारे में सूचित कर दिया है। मुझे अध्ययनकी अवधि और उसके दौरान अपनाए जाने वाले निर्देश भी मेरी भाषा मे समझा दिए गए हैं| मैं उपरोक्त अध्ययन में बिना किसी दबाव के दाखिला ले रहा हूं और पूर्ण सहमति दे रहा हूं | सन्तोष अस्पताल, गाजियाबाद में अपने आगे के उपचार पर बिना प्रतिकूल प्रभाव डाले इस अध्ययन से और प्रयोगशाला जांच की प्रकृति से मैं जब चाहूँ बाहर जाने के अपने अधिकार को सुरक्षित रख रहा हूं |

रोगी / रोगी के रिश्तेदार के हस्ताक्षर

डॉक्टर के हस्ताक्षर

नाम

दिनांक:

मेरी उपस्थिति में मरीज ने पूरी तरह से डाकटर के बताए गए अध्ययन और निर्देशों को समझने के बादअपनी स्वतंत्र इच्छा से ऊपर के फार्म पर हस्ताक्षर किए हैं ।

हस्ताक्षर

नाम: डॉ नितिन आर पिल्लई
पदनाम: पीजी
शल्य चिकित्सा विभाग
संपर्क नंबर- 9847388440

ETHICAL COMMITTEE CLEARANCE

SANTOSH
Deemed to be University
(Established u/s 3 of the UGC Act, 1956)

F. No. SU/2021/1830[49] Dated: 17.07.2021

Subject: Grant of Ethical Clearance for Thesis Protocol Topic **"CLINICO-POTHOLIGICAL FEATURES, MANAGEMENT AND OUTCOME IN PATIENTS WITH CARCINOMA OF ORAL CAVITY A CROSS SECTIONAL OBSERVATIONAL STUDY",** submitted by **Dr. Nithin R Pillai,** MD/MS student of Batch 2020-2021, Department of **General Surgery**.

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With reference to his/her request for grant of Ethical Clearance for the Thesis Protocol entitled **"CLINICO-POTHOLIGICAL FEATURES, MANAGEMENT AND OUTCOME IN PATIENTS WITH CARCINOMA OF ORAL CAVITY A CROSS SECTIONAL OBSERVATIONAL STUDY", Dr. Nithin R Pillai** is informed that the Thesis Protocol submitted by him/her was considered by the **Screening Committee** of the Santosh Medical College & Hospital in its meetings held on 19.03.2021, 22.03.2021, 24.03.2021, 25.03.2021, 26.03.2021, 27.03.2021 and 06.04.2021. The recommendations of the **Screening Committee** were considered in detail by the Institutional **Ethics Committee** in its meeting held on **12.07.2021** and the same was **approved** by the **Ethics Committee**.

He /She is informed accordingly for further necessary action.

[Dr. V. P. Gupta]
REGISTRAR

SANTOSH DEEMED TO BE UNIVERSITY REGISTRAR GHAZIABAD, NCR DELHI

Dr. Nithin R Pillai
MD/MS student of batch 2020-2021
Department of General Surgery
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Copy to:

1. The Vice Chancellor
2. The Dean, SMC&H
3. The Dean – Research
4. The Dean – Academics
5. The Director - IQAC
6. Dr. Gyanendra Mittal (Guide)
7. HOD of **General Surgery**